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The Pathology of Nephritis

as illustrated by thirty-two consecutive cases

BY

WILLIAM OPHÜLS
Professor of Pathology

From the Division of Pathology
Stanford University Medical School

STANFORD UNIVERSITY, CALIFORNIA
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THE PATHOLOGY OF NEPHRITIS

AS ILLUSTRATED BY THIRTY-TWO CONSECUTIVE CASES

It may seem presumptuous on the part of a pathologist to attempt to write a treatise on the Pathology of Nephritis including a resume of the symptomatology of the disease, because the evidence collected from the histories of the patients is necessarily second-hand and incomplete and the author is not trained in the interpretation and evaluation of clinical phenomena. It may be contended, however, that the careful judicious contemplation of a clinical history by some one not connected with the case and not interested in the matter of clinical diagnosis—provided he has the necessary knowledge of Medicine in general—may bring out the salient points in the biology of the disease with greater clearness. However that may be, since it became necessary to consult the records in trying to solve the etiological questions involved, an attempt has been made to give an outline of the progress of the disease in each individual case as briefly as possible, without entering into any of the many details that are chiefly of clinical importance.

The aim has been to collect in each case all relevant data which might have any bearing on the etiology, progress and termination of the disease.[1] To this was added an abstract of all autopsy findings which might be of interest, and an especially careful description of the findings in the kidneys, both in the gross and microscopically. Since no mere description in words can convey an adequate conception of the findings, photographs of the gross specimens have been added wherever feasible, and in all cases photomicrographs of the diseased kidneys. The latter, of course, reproduce only a very small area of the tissues examined; but an attempt has been made to show as much as possible without

[1] The results of functional tests have not been considered, with the exception of an occasional reference to the phenolsulphone-phthalein test. This has been done, not because their great scientific interest and practical value is not fully recognized, but because many cases antedated the use of such functional tests, so that the evidence in the few recent cases is hardly sufficient to warrant any deductions. An attempt to go into this question, in which all clinical workers at present are deeply interested, would also have opened up such a large field for discussion that it seemed wise to refrain from discussing it altogether.

losing all detail, and to select for reproduction as representative places as possible in the sections. The tissues were hardened in Orth's mixture and stained with haematoxylin-eosin, or according to van Gieson's method. In each case several sections were also stained with Weigert's stain for elastic fibers, and with Giemsa's stain for bacteria, and in order to bring out the characteristic granulations of the various leucocytes.

All photographs and photomicrographs are comparable with one another, since all photographs have been taken at about one-half normal size, and all photomicrographs at the same magnification (57 times natural size).

It is hoped that the cases as represented will speak for themselves. The comments which precede them serve the purpose of presenting some of the main facts in a readable manner, and also to draw such conclusions from them as may seem warranted.

The cases, in the opinion of the author, are all cases of true diffuse glomerulo-nephritis, and represent all such cases that were encountered in a consecutive series of about nine hundred necropsies. They are the same cases which were used in preparing the author's previous publication in the *Journal of the American Medical Association* in 1915, where a summary of the findings is given under the headings of acute, subacute, and chronic glomerulo-nephritis. It is unlikely that any case of importance escaped detection, because microscopic sections of the kidneys were examined in all nine hundred cases, and in the vast majority of instances personally by the writer. All cases of chronic parenchymatous nephritis with amyloid disease have been excluded, as also all cases in which the renal lesions were evidently of minor importance as compared with coexisting arterial disease.

For convenience' sake the main data of each case have been gathered in one large table, which is placed at the end of the volume.

A historical review of the subject is purposely omitted, because to cover this part of the subject adequately would consume much space—unnecessarily, it would seem, because the subject has been dealt with extensively and adequately by other writers. Since the author has previously attempted to present what appeared to him the main facts in the historical development of the subject, and has attempted to give due credit for previous work, he hopes to escape the imputation that he attempts to assume more credit than is due for his own efforts. In fact, the author specifically disclaims all credit to himself except that which may be due to the careful presentation of a series of case-reports. His comments are merely expressions of his personal opinion, and are based, naturally, not only on his own observations, but upon the splendid work

done by numerous investigators recently and during the course of the last century.

Since in teaching it is necessary always to go back to the sources of original information, a series of complete case-reports of one particular disease should be of great benefit to teacher and student. It would be especially gratifying to the author if this little volume should prove to be useful for teaching purposes.

I. Acute Glomerulo-Nephritis (Cases 1-4).

The first two patients were males of over 50 years of age, with old infections endocarditis of the aortic orifice. According to the histories, and also according to the anatomical findings, the original infection dated back many years; in the first case, at least eight, and in the second altogether twenty years. The course of the disease in both cases was quite the usual one for chronic endocarditis, and the patients died in one of the exacerbations.

The nephritis in both cases was terminal and incidental to the main disease. In the first case it revealed itself clinically by very definite urinary findings, and by a slowing of the phenolsulphone-phthalein secretion. In the second case the urinary changes were very slight—so much so that the condition might very well have been overlooked clinically.

In both cases diplostreptococci were found in the lesions in the heart valves, and in the first case also in the urine, and in the spleen at necropsy.

The kidneys in these two cases were not as yet very much swollen; the cortex was somewhat opaque, the seat of petechial haemorrhages. The glomeruli showed the very earliest lesions: hyaline necroses of some of the loops, and a very marked infiltration with neutrophilic leucocytes. In case 2 there was some extra-capillary proliferation in the glomeruli, and a slight infiltration of the adjoining connective tissue with neutrophilic leucocytes. There had been much bleeding from the diseased glomeruli, and also escape of some leucocytes into the tubules. There were as yet few casts, and the epithelium was nearly unaltered.

In the case (1) in which the bacteria were found in the urine, no bacteria were found in sections of the kidneys either in the glomeruli or in the tubules; but there were many capillary diplostreptococcic emboli between the tubules, some with beginning suppuration about them. This is one of the cases which so strongly suggest that in glomerulo-nephritis coccus embolism does take place in the glomeruli, but that in these structures the bacteria are rapidly dissolved, in this way causing the hyaline thrombosis and necrosis of the vascular loops.

It is interesting to note that in both of these cases there were quite a few small foci of old *focal* nephritis, such as have been described in diplostreptococcus endocarditis by previous observers. This was also the case in observation 3. Evidently for many years the kidneys withstood the effect of continued bacterial embolism fairly well, until in the end they more or less suddenly gave way. It is difficult to say whether

this should be ascribed to an increased virulence on the part of the infectious organism or to the development of a hypersensitiveness in the organ. It appears to me that on the whole the last view is the more likely one.

The third case is remarkable because, in spite of the fact that an old endocarditis was found at autopsy, there were no clinical symptoms to suggest it. The fourth case is one of cirrhosis, with the usual clinical manifestations. In both of these last cases the acute nephritis developed in the last three weeks. In case 3 there was a very suggestive history of a sudden breakdown, with characteristic disturbances in urination three weeks before his death. The patient suddenly had to urinate very frequently, and developed oedema. In case 4 there is no such definite history of the onset, but about a month before her death she became much worse, this being some time after the development of septic ulcers on her legs, which were probably the cause of her nephritis. The nephritis in these cases is therefore probably about three to four weeks old. Clinically it showed by the development of oedema. Some puffiness of the face is recorded in case 4. The urine in both cases contained much albumin, many hyaline and granular casts, and some leucocytes.

The kidneys were greatly swollen. They were hyperaemic and oedematous. The cortex was wide, more or less yellowish, and opaque. It contained petechial haemorrhages. Histologically there was somewhat more evidence of extracapillary proliferation in the glomeruli: otherwise the lesions were similar to those observed in the earlier cases. Many tubules were filled with blood and with neutrophilic leucocytes. The epithelium was swollen, somewhat granular, and in one case fatty degeneration had occurred. The interstitial tissue in both cases was heavily infiltrated with neutrophilic leucocytes and with lymphocytes. In case 4 there was already evidence of a beginning proliferation of the connective tissue cells. That this proliferation was of inflammatory origin is so evident that it does not admit of any discussion. In some of the glomeruli also a beginning organization of the necrotic material had set in. In the one case in which the tissues examined were sufficiently well preserved for bacteriological examination no bacteria were found, in spite of long continued search with the mechanical stage through several sections.

In all four cases of acute glomerulo-nephritis the etiology was clearly evident. There was streptococcic infection with bacteriaemia in all, and in three the nephritis occurred in the final stages of an old diplostreptococcic endocarditis. The death of these four patients is largely attributable to their pre-existing disease, and it was for this reason that

there was an opportunity of studying the alterations in the kidneys at this early stage.

In the very beginning the lesions are practically confined to the glomeruli, the initial change being a hyaline thrombosis of some of the vascular loops, followed by necrosis and an infiltration of the entire glomerulus with neutrophilic leucocytes. Naturally in ordinary sections not all affected glomeruli show the necrotic loops, but my impression is that in a series one can always find them in each affected glomerulus. The diseased glomeruli bleed and permit of the passage of albumin and leucocytes—which explains the material found in the capsular spaces, in the tubules, and in the urine. Sometimes the exudate has a tendency to spontaneous coagulation in the capsular spaces and in the tubules.

Very soon these glomerular lesions are followed by a general hyperaemia and oedema which causes considerable enlargement of the organ. The oedema often is very pronounced. The hyperaemic blood-vessels show a marked local leucocytosis, numerous venules in the region of the vasa recta being especially engorged and full of various types of leucocytes. The congestion is soon followed by a general extravasation of leucocytes into the tissues, the intensity of the reaction naturally depending on the severity of the process. Among the leucocytes that find their way into the tissues there are many neutrophilic cells, together with lymphocytes and plasma cells, as can easily be seen in sections stained with Giemsa's stain according to Schridde's method. The amount of epithelial degeneration also naturally varies with the intensity of the process. In some of our cases it is noted as slight, in others it is quite considerable. There is no question that the disturbance in circulation and the oedema as such must be important factors in the development of these degenerative lesions; still one can hardly escape recognizing also the importance of a toxic factor. The possible epithelial lesions at this time consist in swelling, with slight granular degeneration, fatty degeneration, and scattered necroses.

As a result of the inflammatory oedema the connective tissue cells of the interstitial tissue become swollen. After a few weeks, evidences of proliferation may be observed on their part. As has been stated above, of the inflammatory nature of this proliferation there can be no doubt.

In the glomeruli also proliferative changes occur quite early in the process. The capsular epithelium swells, is partly detached, and proliferates somewhat. My impression, however, is that the majority of the new cells in the glomeruli which become so plentiful in the later stages are derived from the connective tissue, both of the capsule and of the

stalk of the glomerulus. The proliferative process in the glomeruli also is partly distinctly inflammatory; in part, however, it is in the nature of an organization of the necrotic material produced, or of deposits of fibrin which are apt to occur in the capsular space.

Of the origin of the apparently initial hyaline thrombosis and necrosis of some of the vascular loops of the glomeruli, I have spoken at length in my previous article. Suffice it to state here that it appears probable to me that it may be due to rapid lytic destruction of bacterial emboli, with liberation of haemolytic and necrotizing endo-toxins.

The slight lesions in the larger arteries in the kidneys and elsewhere which are noted in the protocols, are naturally purely incidental.

I may state at this point that for brevity's sake in the protocols I have used the terms "arteriosclerosis" and "endarteritis" in the sense of Jores, employing "arteriosclerosis" when there was a notable hyperplasia of the elastic elements of the intima. The distinction, however, is meant to be a purely morphological one, not implying the deeper significance attributed to it by Jores.

II. Subacute Glomerulo-Nephritis (Cases 5-12).

Naturally, there exists no sharp line of division between the acute, subacute, and chronic cases. Cases 5 and 6, for instance, might just as well have been classified with the acute, and cases 11 and 12 with the chronic types.

The beginning and the course of the disease were very characteristic in case 5. The patient's trouble commenced with an attack of tonsillitis about nine months before she died. Soon symptoms of acute polyarticular rheumatism made their appearance, and continued intermittently for about six months. The severe endocarditis, which evidently developed simultaneously, was overlooked until the patient entered the hospital in the last stages of the disease. At that time she already showed evidence of severe renal involvement. It is not apparent from the history when her renal disease started. How far her oedema was associated with her nephritis is difficult to tell; but there are certain symptoms recorded in the history, like frequent vomiting, restlessness, drowsiness, muscular twitching, which arouse the suspicion of a uraemic condition. Her blood pressure, in spite of the severity of her renal complication, was not affected, possibly on account of the severe septic involvement of the heart muscle. Diplo-streptococci were recovered during life from blood and urine, and after death from the infected heart valves.

The following case (6) is an interesting one on account of the fact that the infection which caused the nephritis was apparently caused by colon bacilli, no evidence of streptococcus infection being discovered either during life or at necropsy. On account of the fact that the child had congenital syphilis, it might be suggested that the lesions in the kidneys also were of syphilitic origin; but so long as we know so little of the histology of acute and subacute syphilitic nephritis, I believe we would hardly be warranted in making this assumption. In other words, I do not believe that the proof has yet been furnished that spirochetes can produce lesions in the kidneys similar to those observed in ordinary bacterial infections.

The next case (7) is a good example of how inattentive some patients are to the state of their health. The first symptom that attracted this patient's attention was a hemiplegia and aphasia as a result of embolism from a severe diplostreptococcus endocarditis. The urinary findings were unusually slight for the severe lesions in his kidneys. Except for the general oedema, which of course may be attributed to his cardiac disease, there were no other general symptoms of nephritis.

In patient 8, who had an old streptococcus infection of a compound fracture of the leg, the urinary findings made the diagnosis of nephritis evident. There was some oedema, but it was not very marked at any time. Other "nephritic" symptoms were completely absent, in spite of very severe lesions in the kidneys.

In case 9 the renal disease was only a minor incident in the typical clinical development of a severe septic endocarditis, probably arising eight months before death from infected wounds on the fingers. Still, the urinary findings were unmistakable and the phenolsulphone-phthalein excretion was distinctly slowed. Three months before his death the patient had noticed some oedema at the ankles, increased thirst, and increased urination. The oedema at no time was a prominent symptom, and was absent at death.

Case 10 is noteworthy in several particulars. The patient, a young woman, had had an unusually severe long-continued infection, developing from a decayed tooth about one year before her death. An abscess eventually formed at the lower jaw which had to be drained from the outside. Following the operation the abscess healed, and at necropsy a small scar only could be found at the place where it had been. Several decayed teeth, however, remained in her mouth. After the healing of the abscess she was apparently well until four weeks before her death, when she developed a painless oedema of the legs. Ten days later the right leg, which was still oedematous, became infected with streptococci, from which infection she died within a short time.

The histological picture of the lesions in the kidneys in this case differs from that of other cases of this series by the lack of evidence of actively progressive inflammation. The alterations were very extensive, but apparently not very severe, and almost quiescent. Almost all of the glomeruli were diseased. They showed development of fibrous tissue between the vascular loops, making the tufts thick and heavy. There was also some little proliferation in some of the capsules and in the capsular spaces. Although so many glomeruli were diseased, one did not receive the impression that the majority were functionally badly damaged. The newly formed fibrous tissue was found on the inside of the tufts, and did not therefore apparently interfere much with the secretion of the urine-water; and the vascular loops themselves, although some of them showed a slightly thickened hyaline wall, appeared otherwise normal. Many tubules were filled with hyaline casts, and some of them with neutrophilic leucocytes. The epithelial degeneration which was present in the tubules was probably recent, and to be attributed, at least in part, to the streptococcus sepsis from which the patient died. The

arteries were practically normal, except the main stems of the renal arteries, which were moderately sclerosed. On the whole, therefore, the histological picture would suggest that the process was fairly well healed, at any rate rather quiescent. Clinically, however, the evidences of renal disease were well marked. Her first symptom, the oedema, was evidently a "renal" oedema, because there were no signs, either clinical or anatomical, of cardiac decompensation. There was also distinct hypertension, and a slight but unmistakable hypertrophy of the left ventricle. The urinary findings also were well marked. Although the urinary production was diminished, the specific gravity was fixed at about 1010; there was much albumin in the urine, and many formed elements in the sediment. Symptoms of uraemia, however, were altogether absent.

In the following case (11) we have subacute nephritis in an individual suffering at the same time from old diplostreptococcic endocarditis and syphilitic aortitis with aneurysm. The time when the diplostreptococcus infection took place cannot any more be established exactly, but the patient complained of heart trouble for at least four years before his death. As shown by a history of extreme polyuria half a year before his end, his nephritis must have dated back before this time. The polyuria in this case was a striking and constant symptom, and possibly accounts for the comparative absence of oedema. His symptoms were largely those of endocarditis, complicated naturally by the co-existing aortic aneurysm. His blood pressure was high and rising. His heart was twice normal size, an enlargement partly due to aortic regurgitation. His urine, on account of the polyuria, naturally had a constant low specific gravity; it contained much albumin and many formed elements. While he was at the hospital there was practically no excretion of phenolsulphone-phthalein. The pericarditis which he developed eventually was due to an extension of the diplostreptococcic infection from the heart valves to the pericardium.

In the last case (12) the nephritis is evidently much older than in the others of this series. This patient had had numerous attacks of tonsillitis from infancy. Six years before death her nephritis had been first noticed. For the last five years she had had definite "uraemic" symptoms (headache and vomiting), and occasionally slight oedema. The most interesting feature in this patient's history was that she had associated with her nephritis what appeared to be typical symptoms of "Raynaud's disease," attacks of syncope and cyanosis in fingers and toes. Eventually she developed an anaemic (?) contracture of her left arm and a dry gangrene of her left foot. This symptom-complex was probably due to a gradual closing of her peripheral arteries by lateral thrombosis and endarteritis. Unfortunately we were not permitted to verify this sup-

position at autopsy; but we have evidence that her internal arteries, more especially those in the heart and kidneys, were gradually being closed by such a process. In both of these organs, as a consequence, small multiple necroses resulted, which in the heart were irregularly scattered, and in the kidney were situated in the pyramids. Bacteria were not found in the small arteries which were the seat of the thrombosis. Towards the end a similar thrombotic obstruction took place in some of the arteries of the sigmoid flexure, with much bleeding and extensive sloughing. All these processes naturally at first suggested the occurrence of multiple embolism; but no source of embolism was discovered in the pulmonary vein, left heart, or the aorta; besides, the gradual development of the conditions in the extremities speaks very much against embolism as the causative factor, and favors the idea of their origin by gradual thrombosis.

The case, I believe, is of unusual importance, because it seems to furnish the proof that the lateral thrombosis followed by endarteritis, which is so frequently observed in the kidneys in these cases of glomerulo-nephritis (see below), may involve arteries in other parts of the body, and may in this way give rise to symptoms resulting from a more or less gradual obstruction of them. No doubt sometimes the cerebral arteries may be involved in the same way. That this patient, in spite of the absence of an infectious endocarditis, suffered from a chronic diplostreptococcus bacteriaemia, at least as long as she was under clinical observation, seems evident. She had a septic temperature all the time. Her pulse rate varied between 80 and 130, and the blood culture was positive. In fact, clinically there seemed to be no doubt that the patient had a septic endocarditis, and the absence of this condition at autopsy was a great surprise. Unfortunately, a thorough search for another chronic septic focus could not be made. It is possible that in this instance the urinary tract itself may have harbored the diplococci, because there was evidence at necropsy of a slight chronic suppurative pyelitis and cystitis with positive finding of diplostreptococci. This, however, may have been merely the consequence of the constant elimination of diplostreptococci by way of the kidneys.

This patient's "nephritic" complications were unmistakable. She had headaches and vomiting; she had albuminuric retinitis; she had comparatively little oedema; she had a high blood pressure with clinical signs of excessive heart action, but without gross hypertrophy; she died in uraemic coma. The urinary findings also were very well marked. She had some symptoms suggesting polyuria, a fixed low specific gravity. The urine contained much albumin, and at times there were large showers of casts. Red blood cells were also commonly found.

To sum up: In all these cases of subacute nephritis, except in case 6, there can hardly be any question of the etiology; and in this one I am inclined to believe that the nephritis was due to a colon bacillus septicaemia arising from the infected urinary tract. In the cases with endocarditis (5, 7, 9, 11) chronic diplostreptococcus septicaemia existed, without doubt; in case 8 a chronic streptococcus septicaemia from the infected bone is also very likely; and in case 12 the clinical symptoms and the positive blood culture proved the existence of a chronic septicaemia, at least as long as the patient had been under clinical observation. The source of the continued infection in this case was possibly in the urinary tract. The only somewhat questionable case is case 10, where the original septic infection was present in the region of the jaw, where, however, after long treatment the lesion eventually healed. No persisting septic focus was definitely made out, although she still had several decayed teeth; and it is possible that the histological evidence of comparative quiescence of the process in the kidneys might indicate that whatever infection remained was not very active or extensive.

The clinical symptoms of nephritis were quite definite in all cases. All of them had oedema at one time or another, the amount of oedema and its distribution varying very much in different cases. One early case (5) had somewhat indefinite symptoms of uraemia; otherwise the others were free from it, except the most chronic case, which was much older than the rest, in which there were observed very definite uraemic symptoms and a well marked retinitis albuminurica.

Case 8, of about six months' duration, already showed a beginning hypertrophy of the left ventricle; and the last three cases had a definite rise of systolic blood pressure to between 170-200 mm. mercury, and two of them a noticeable hypertrophy of the left ventricle. In the case (11) with very marked hypertrophy of the heart, the hypertrophy was probably largely due to valvular disease.

The urinary findings were striking in all cases. The urine at all times contained much albumin. Casts (hyaline, granular and epithelial) were almost just as constantly present, although sometimes they were not found at all times, but in showers. Leucocytes and erythrocytes, either free or as blood casts, were also commonly encountered. Two cases (9 and 11) had a definite polyuria, which was extreme in case 11. In the more chronic cases (10, 11, 12) the specific gravity was fixed at a low point, not always apparently as a result of polyuria, the condition being suggestive of a true hyposthenuria.

In case 9 the phenolsulphone-phthalein excretion was somewhat slowed, in case 11 entirely suppressed, and in case 12 very much delayed.

In the gross, the kidneys were smooth, congested, oedematous and swollen, or already contracted to about normal size. The cortex was either diffusely opaque or contained small opaque spots. Petechial cortical haemorrhages were often seen. They were most numerous in case 5 (see fig. 7). Histologically, in the more acute cases the tissues were still much infiltrated with neutrophilic leucocytes, to which were now added many eosinophilic and basophilic cells. The glomeruli in most cases showed a very general intense intra- and extra-capillary proliferation. In the more chronic cases many of them had already become fibrous. The tubules were full of blood, neutrophilic leucocytes, and casts. The amount of degeneration in the epithelium of the tubules varied, being intense in some cases and rather light in others, without much reference to the severity of the lesions elsewhere. In all cases the interstitial tissue, in addition to being infiltrated with lymphocytes and granular leucocytes, showed evidence of considerable fairly diffuse, inflammatory proliferation, which in the later stages had already commenced to encroach upon the tubules in some places.

The arteries in the kidneys were normal in cases 5, 6, 7, and 9. In case 8 the slight arterial lesions were evidently purely incidental, which is probably also true in case 10; but in case 11 definite lesions were found in some of the arterioles and larger blood-vessels, which must be associated with the nephritis; and in case 12 the arterial involvement was unusually well marked. The lesions in these last cases seem to extend back from the affected glomeruli into the arterioles, and to consist in lateral hyaline thrombosis, with rapid organization leading to endarteritis. In the cellular newly-formed connective tissue in the intima there are practically no elastic fibers, as is well shown in fig. 18. In the larger arteries, on the other hand, there is no evidence of such a process; but there is present a definite hyperplastic thickening of the elastic tissue of the intima.

The arteriosclerosis found in other parts of the body in cases 8, 11 and 12 can almost certainly be looked upon as being unconnected with the renal disease. Cases 10, 11, and 12 demonstrate clearly that the blood pressure rises and remains constantly elevated before there are anatomical signs of general arterial disease. The rise in pressure must be due to some functional disturbance in arteries and heart, which throws out of action the regulatory mechanism which normally maintains the blood pressure at such a remarkably constant level.

The anaemia which was present in all cases is in all probability to be attributed to the chronic sepsis, rather than to the disease of the kidneys.

III. Late Subacute Glomerulo-Nephritis in Children (Cases 13-15)

The following three cases are of special interest because they show the effects of continued nephritis on the youthful organism. The patients were children between 6 and 10 years of age. The possibility of arteriosclerosis complicating the condition can be positively excluded in these cases, and as a matter of fact no general disease of the blood-vessels was observed in any of them. Whatever cardio-vascular disturbances were observed in these instances must therefore be in some way associated with the disease in the kidneys.

The first of these cases (13) had no history of any acute infections except the milder types of diseases of childhood. The possibility of her having had an attack of tonsillitis, rheumatism or scarlet fever was positively denied on repeated questioning, which is remarkable and shows that the diplostreptococci sometimes enter without provoking severe symptoms, because at necropsy it was discovered that she did suffer from an old diplostreptococcic infection of the aorta.

Her first symptoms, five months before death, were of a uraemic nature, of that type which gives rise to headaches, vomiting and convulsions. The convulsions in this patient were not very severe. They were frequently followed by periods of amaurosis, probably due to spasm in the retinal artery.

In addition to this functional and more or less transitory condition, organic lesions later developed in the fundus of her eyes; optic neuritis and retinitis, and a detachment of the retina in the left eye. After a while increased thirst and polyuria was noticed. She had remarkably little oedema of the skin (slight puffiness of the face at one time). Her polyuria with low specific gravity continued to the end. Otherwise the urinary changes were not very pronounced; the urine containing little albumin, few casts, and some leucocytes. Her systolic blood pressure was about 140. The clinical signs were pre-eminently those of a severe sepsis (continued fever and leucocytosis), and the general findings and also the local ones in the region of the heart again suggested strongly endocarditis, as in case 12. Contrary to all expectations, no endocardial lesion was discovered at autopsy, but an infectious aneurysm in the upper part of the abdominal aorta in which there were numerous diplostreptococci, and a severe glomerulo-nephritis with considerable shrinkage of one kidney.[2] The cardiac hypertrophy which had been noticed clinically

[2] The only clinical symptom of the aneurysm had been obscure pains in the upper abdominal region.

and had been ascribed to the suspected endocarditis, turned out to be due entirely to the "nephritic" hypertension. In this case the arteries were normal, grossly and microscopically, in kidneys and elsewhere, with the one exception of the arterioles in the spleen.

Patient 14, a girl of 10 years, had had frequent attacks of tonsillitis. She had a septic temperature on a subnormal base at about 96° F, also continually some leucocytosis; but the old septic focus, which evidently existed somewhere in her body, was not discovered at autopsy. The first symptoms, which appeared two years before death, were more of a cardiac nature (precordial pain and dyspnoea); and in her last attack the symptoms of broken compensation were the prevailing ones. Towards the end she was very restless and in a semi-comatose condition, probably as a result of true uraemia. Her blood pressure was quite high (160) for a child of her age, and the necropsy revealed marked hypertrophy of the heart, which was especially well developed on the left side. The urine contained much albumin and rather few casts, also a few erythrocytes occasionally.

The last one of these cases (15) showed a definite localization of the septic focus in the urinary tract. The involvement of the kidneys was not due to ascending infection, but it was in the nature of a true haematogenous glomerulo-nephritis (see fig. 27). Two years before this little boy's death a large stone was removed from his bladder. At that time already infection of his bladder was evident, and this infection with streptococci continued to his end. Cardiac and renal symptoms (polyuria) developed five months after the operation, and he died in uraemic coma. In this case also the cardiac hypertrophy was well marked, more especially on the left side.

In these three cases of late subacute nephritis in children, then, the cardio-vascular disturbances were very prominent clinically, and the cardiac hypertrophy well developed anatomically. Cases like these furnish the best proof that the hypertension is closely associated with the disease in the kidneys, but does not necessarily depend upon the extent of destruction of renal tissue. In case 15 the amount of functionating renal tissue left is very small; still the cardiac hypertrophy is quite insignificant in comparison with that observed in case 13, in which the damage to the kidneys is evidently much less extensive. In the growing body of a child the response of the heart muscle by hypertrophy to the increased work seems to be unusually rapid and extreme. That arterial spasm plays some rôle in the production of the hypertension is strongly suggested in case 13, in which the tendency to spasmodic contraction was so well marked in the retinal artery and was directly observed by means of the ophthal-

moscope. If, from the behavior of this one artery, one could arrive at a definite conclusion as to the state of the rest of the small arteries, the evidence would, of course, be more convincing; but unfortunately such is not the case.

Oedema was observed in two of these three cases, but it was not a prominent feature in any of them. Clinically a certain puffiness of the face was practically all that was noticed. In the last case, at autopsy all tissues were found to be unusually dry. In this connection it is interesting that the existence of a polyuria is especially emphasized in the records of cases 13 and 15. In case 14 it had been unfortunately impossible to determine the amount of urine. In cases 13 and 14, however, ascites and hydrothorax developed in the end.

In case 13 the urinary findings, apart from the polyuria, were unusually slight. Repeated examinations failed to reveal anything more than a small amount of albumin and occasionally a few hyaline casts. The albumin was much more plentiful in case 14, but here again the number of casts was limited. In case 15 the condition of the urine is unknown.

"Uraemic" symptoms were present in all three cases. The symptoms of the first patient started with headache and vomiting, and there were imperfectly developed convulsive attacks. Whether she eventually developed true uraemia and coma is unfortunately unknown. That this condition was present in case 14 is very probable from the history, and certain in case 15.

Whether the changes in the backgrounds of the eye which were observed in case 13 can be included in the usual picture of retinitis albuminurica is doubtful.

The anaemia which usually accompanies chronic sepsis and nephritis was present in all cases, but to a moderate degree only.

The kidneys, except for the one large kidney in case 13, were irregularly contracted. In cases 13 and 15 they showed large, deep, irregular scars; in case 14 they were more finely granular. The unusually small size of the one kidney in case 14 is probably partly due to disturbances arising from the stenosis of its ureter by a congenital fold.

The microscopical appearance of the lesions was very much that which has been described in the later cases of subacute nephritis in adults, only that in cases 14 and 15 in places the development of the fibrous tissue was more massive and the atrophy of the tubules in these areas further advanced, as is well shown in figures 25 and 28. The inflammatory character of the connective tissue proliferation was again very evident in all cases. Many glomeruli were already entirely fibrous, more especially in the older lesions.

It was case 15 which first demonstrated to me the fallacy of the belief that from the appearance of the glomerular remnant one could determine whether the glomerulus was thrown out of function by arteriosclerosis or whether it was destroyed by glomerulo-nephritis. It is true that in the latter case the fibrous remnant is usually badly defined and has lost all semblance to a glomerulus, whereas in arteriosclerosis the vascular tufts merely collapse and are surrounded by a more or less crescent-shaped thickened hyaline capsule. If in glomerulo-nephritis the lesions are mostly capsular, however, a very similar condition to that which occurs in arteriosclerosis may be observed in the end. This may be very puzzling, especially when it is associated with much endarteritis, as in case 15. It is for this reason, I believe, that many cases have been classified as arteriosclerotic nephritis which really belong to glomerulo-nephritis.

The local condition of the arteries again varied remarkably in this short series. In case 13 they were entirely normal. In case 14 the small arteries showed a well marked "endarteritis," and in some of the larger ones the internal elastic membrane was split up into several thick superimposed layers, giving the typical picture of a hyperplastic development characteristic of true arteriosclerosis according to Jores. In case 15 the lesions in both small and larger arteries were in the nature of a very pronounced "endarteritis."

IV. Chronic Glomerulo-Nephritis (Cases 16-32).

In order to avoid tedious repetition the cases of this last series will be taken up in a more summary fashion.

Ever since the disease has been recognized the etiology of these chronic cases has been a most vexing problem. Whereas in the acute and even the subacute cases the history of some septic infection can usually be obtained and a persisting septic focus can often be demonstrated fairly easily, in the chronic cases the history of the original infection dates back so far that it often is entirely forgotten by the patient, especially by patients who are more or less indifferent in regard to the state of their health; and the persisting focus apparently may be so insignificant that an unusually careful clinical examination and even an unusually carefully performed necropsy may fail to reveal it. In these cases the original infection is probably often due to organisms of a low degree of virulence which provoke very slight symptoms, and the bacteriaemia also is comparatively slight and intermittent, as one would expect from a comparatively insignificant and hidden focus.

In searching for the time and character of the original infection the question, how far one is able to communicate with the patient and his family, is of great importance; so that in patients able to speak foreign languages only, especially such languages as Chinese and Japanese, it is often a practically hopeless task. Many of these patients arrive at the hospital in a comatose condition, and, unless close relatives or friends are accessible, very little or nothing can be made out about their antecedents.

Among our sixteen cases there were seven (cases 16, 18, 20, 25, 27, 29, 32) in which for one reason or another the history is imperfect. Of the other nine patients one (17) had scarlet fever as a child and rheumatism at twenty years of age, another (19) claimed to have been healthy all his life. He even denied having had any diseases in childhood, which makes his statements somewhat improbable. Patient 21 had had a severe infection, "a touch of typhoid," as she said, at the age of 22, and her symptoms dated from the time she was 23. Patient 22 had had a long continued suppuration of the neck due to chronic tuberculosis, necessitating twelve operations. In such a case the existence and persistence of mixed infection with septic organisms is, of course, not at all unlikely. In the history of patient 23 we read of repeated attacks of tonsillitis and several attacks of polyarticular rheumatism. Patient 24 also has a history of rheumatism. In case 26 we encounter once more a

general denial of all diseases except measles in infancy. In case 28 also there is no statement in regard to the original infection. Patient 30 had had frequent attacks of sore throat, and patient 31 had had what she called "La Grippe" as a girl and an attack of acute appendicitis nine years before her death. A direct relation of the original infection to the following nephritis is traceable only in one case (21); still the investigation shows that in fully six of the nine cases the existence of some infection preceding the nephritis and likely to provoke nephritis, could be established.

The mere presence of such a history does not of course prove that the nephritis must have been due to such infection. However, in this connection we have to consider that in all acute and subacute cases the relation of such infections to the nephritis is very evident; and there is no reason to assume that the chronic cases of evidently the same disease should be due to a different cause. Considering the difficulties, I believe that the finding of a history of a suspicious infection in six out of nine complete histories is quite suggestive—all the more so, as in one of these negative cases (28) in spite of the denial of all infection and in the absence of any symptoms observed by the patient, a chronic infectious endocarditis was found at autopsy.

Definitely persisting septic foci were found in the sixteen cases as follows: old atheromatous ulcers infected with diplococci in case 16; old pus pockets in the tonsils with considerable scarring in case 20; an old healed scar at the base of the aorta and an old septic infarct of the spleen full of influenza bacilli in the patient (21) who had had a "touch of typhoid" thirteen years before her death; an old ulcerative endocarditis in the patient (23) who had a history of tonsillitis and rheumatism; an old ulcerative endocarditis in case 28; an old ulcerative tonsillitis and an apparently old mild suppurative pyelitis in the patient (31) who had had the attack of "La Grippe." The long continuance of the rheumatic infection in case 17 is shown by the fact that many years after his original trouble he developed a pleurisy, evidently on a rheumatic basis, because there was no evidence of tuberculosis found at autopsy. It is also to be noted that during the last years of his life he complained for several years of chills in the evening and night sweats. In case 32 there is a history of "malaria," so frequently wrongly diagnosed in chronic sepsis; and in case 30, with a history of tonsillitis, there is a subsequent history of repeated attacks of arthritis, which may, however, have been gouty in character.

Altogether of the sixteen cases there are six only which are entirely negative so far as history and autopsy findings are concerned; and of

these, four have imperfect histories. One of these (19) had a chronic suppurative catarrh of the rectum due to diplostreptococcus infection, and a diplostreptococcus sepsis at autopsy. There was no way of determining the age of this infection, because the infection of the rectum had not been noticed by the patient, but was accidentally discovered when a routine examination of the rectum was made after he had entered the hospital.

No really careful examination of the nose, the accessory sinuses, the roots of the teeth, and other well known foci of chronic septic infection, was made in these cases either clinically or anatomically; and I believe the result should encourage us to search more carefully for such conditions. Even under the most favorable circumstances we can hardly hope, in a disease which often lasts twenty years and more, to definitely establish its relation to chronic sepsis in more than a majority of cases. My impression is, that the original infection usually takes place at a comparatively early age (fifteen to twenty years and longer before death), and, as is clearly shown in several of the histories, is unfortunately not immediately followed by clear symptoms of nephritis, the earliest symptoms (possibly indicating renal disease and consisting of headache and vomiting) having been observed about one year after the infection in case 21. Otherwise the damage to the kidneys is not noticed at the time, nor the persistence of the infection in some more or less hidden focus. Whether a careful clinical examination at the time, with urinanalysis, etc., would reveal the seriousness of the condition remains to be seen, but does not seem at all unlikely.

In such an early discovery of the real seriousness of the situation would consist the only hope of the patient for a permanent cure, by the possible eradication of the septic focus, a general treatment directed towards increased resistance to infection, and a careful symptomatic treatment of the disease of the kidneys. My belief is, that the acute nephritis in scarlet fever is so rarely followed by chronic nephritis, because in the first place the septic infection in scarlet fever is self-limited, and if the patients recover, heals completely; and secondly, because the patients usually are in bed under professional care and the nephritis often is severe enough to be noticed easily, both of these latter circumstances assuring proper treatment. In the more obscure septic infections neither the original disease nor the nephritis which is associated with it may attract sufficient attention on the part of the patient, or of the physician if the case happens to be brought to the attention of a professional man.

The time at which the first definite "renal" symptoms make their appearance varies very much. In case 21 they seem to have followed the

original infection within the year, but usually ten years or more seem to elapse before they become at all prominent. The patients most commonly noticed them from two to five years before death; but in some, in which the disease, from the appearance of the kidneys, must have existed for many years, the complaints of the patients did not commence until four to five months before their end (see cases 28 and 29).

In practically all of our cases the history, when complete enough, contains quite definite evidence of renal disease, with the one exception of case 30, in which there is a fairly typical history of gout, but otherwise nothing suggestive of disease of the kidneys except the one complaint that he had to urinate frequently and had to get up several times at night. Curiously enough in this case the urinary findings also were very slight; both in spite of the fact that the lesions in the kidneys in the gross and histologically were unusually severe (see fig. 50).

There is another case (22) in which the only symptom for the last three years before death was occasional nycturia.[3] A rather common initial symptom was oedema, which in several cases commenced in the face, but not so rarely at the ankles. The time of onset of this initial symptom varied greatly.

In case 16 oedema of the face and legs developed three years before death, and since then recurred at intervals. Similarly in case 17 oedema and dyspnoea made their appearance two and one-half years before the end. Facial oedema was not observed until considerably later. In patient 20 the first symptoms manifested themselves four years before he died, and consisted of general oedema and ascites. In this case the oedema disappeared completely, to return slightly for a short time two months before death. All that was left eventually was some puffiness about the eyes. In case 22, as stated before, the only symptom for several years was occasional nycturia. It was only quite late in the disease that he developed marked oedema of the lower extremities, with very marked dyspnoea and cyanosis. Case 24 started in with dyspnoea and increasing weakness two years before his death. The dyspnoea again was a prominent feature in his last attack in which some facial oedema was observed; but there was no other oedema at any time. Patient 26 became dropsical as early as five years before his death, and had another similar attack four years later. In addition he complained of dyspnoea, palpitation of the heart, precordial pain, headache and pains in the legs. Patient 29 had noticed puffiness of the face, swollen legs, shortness of breath, palpitation of the heart, and precordial pain for about four to five months.

[3] The word "nycturia" in this paper is used as meaning urination at night, and is not meant to refer to involuntary urination.

There is no history of a previous attack, but the data are incomplete. In case 31 the exact nature of the renal symptoms which were first observed when she was pregnant five years before death is not stated; but in her subsequent history oedema is not a very prominent symptom.

In six cases, then, oedema was an early and prominent symptom.

Dyspnoea, as may be seen from the above, was often noticed very early, and this symptom frequently was very severe, out of all proportion to any disturbance in circulation that might have been present. In case 28 it was an early and apparently the most prominent clinical symptom, not associated with oedema or any more definite "uraemic" manifestation. It is not at all improbable that the attacks of "asthma" in case 19 which preceded the end by four years were of this nature. In this patient it was years later that oedema first developed, and he died, similarly to case 28, in extreme dyspnoea.

Palpitations of the heart were quite frequently complained of, and in a few instances there was quite a little precordial distress, sometimes suggesting angina pectoris. The patient in whom this symptom was most prominent (17) had an unusually well marked general arteriosclerosis. The right coronary artery was almost closed at one point, but there were no scars in the heart muscle. In case 26, with similar symptoms, the necropsy also revealed marked arteriosclerosis of the coronary arteries. In cases 21 and 29, however, in which anginoid attacks were complained of, there were no lesions in the coronary arteries or in the heart muscle, and merely a few small yellow spots in the base of the aorta. On the other hand, in case 18, in which there were small scars in the musculature of the left ventricle, no local symptoms were complained of. Patient 24, in whom the heart muscle was similarly affected, also did not complain of any subjective symptoms in the region of the heart, but clinical examination revealed an absolute arythmia. (It may be stated that the heart muscle, like all other important organs, was examined microscopically in all cases.)

In a certain number of cases "uraemic" symptoms occurred early and often dominated the clinical picture. In the early stages the convulsive form of uraemia, characterized by headache, vomiting, and, in extreme cases, convulsions, was usually encountered. Towards the end the symptoms of true uraemia made their appearance, often terminating in coma.[4] In case 17, for instance, the first symptoms two years before death were headache, dizziness, loss of memory, failing eyesight, shortness of breath, progressive weakness, and frequent urination. This man

[4] A discussion of the different forms of uraemia cannot here be attempted, and the reader is referred to the voluminous literature on this subject.

never had any oedema, except slight puffiness of the eyelids. He had a retinitis albuminurica, uraemic convulsions, and died in coma. The symptoms of patient 21 started thirteen years before her death with intense headache and vomiting. She had much oedema at times, and eventually developed symptoms of true uraemia. In case 23 the uraemic convulsions were evidently mistaken for epilepsy. When he came to the hospital, he complained of shortness of breath, increasing dimness of vision, cramps in the legs, and deep pains in the bones. He never had any oedema, and died in uraemic coma.

In other cases again the uraemic symptoms were a late development, as in patient 20, who first had considerable oedema. Later the oedema was much less marked, but he had intense headaches with vomiting, became severely dyspnoeic, was intensely hypersensitive all over his body, especially to deep pressure, and died in an attack of excessive dyspnoea. The patient (22) in whom frequent urination, especially at night, was the only symptom for several years, eventually developed an intense dyspnoea, had some oedema, and died in uraemic coma. In patient 31 the exact symptoms of her earlier attacks are unfortunately unknown. One year before death she noticed anorexia and vomiting. Later she had some attacks of violent delirium, associated with complete unconsciousness. For the last seven months she had headache, much vomiting, jerkings and cramps in legs, progressive amaurosis, and at times oedema of the feet. Ophthalmological examination showed the typical picture of an albuminuric retinitis. The symptoms of true uraemia continued to her death.

Retinitis albuminurica was observed in the above mentioned two cases only. In case 23, in spite of the failing vision, the backgrounds were normal. The retinal arteries were slightly tortuous, and the disturbance may have been due to this patient's severe anaemia, associated with arterial spasm.

All patients, with few exceptions, suffered from severe anaemia. About half the normal number of erythrocytes, or less, and a corresponding decrease in haemoglobin, was observed in cases 17, 19, 20, 23, 24, 28, 29, 30, 31. In several of these cases there was a marked anisocytosis. Associated with the anaemia there was frequently observed a tendency to bleeding in skin and mucous membranes, assuming at times the severity of a haemorrhagic diathesis.

The temperature was either normal or often subnormal, with occasional rises to 99° or 99.5° F. The pulse rate was either normal, or as in case 29 rather slow (between 60 and 80), but in quite a number of cases it varied considerably, and occasionally rose to 100 or even 120.

These disturbances in pulse and temperature are probably due to the associated septic conditions. It is of some interest that in case 21, in which an old septic infarct heavily infected with influenza bacilli was found in the spleen, the temperature was normal, but the pulse rate varied a great deal and sometimes rose to 120.

In practically all, but more especially in the uraemic cases, the tongue in the last stages of the disease was heavily coated and the breath was foul. In some of them a severe pseudomembranous and ulcerative stomatitis developed eventually, which in case 16 was mistaken for diphtheria, because it started in the region of the tonsils and gave rise to the formation of greyish membranes. The lesions usually, however, are much more widely distributed than those of diphtheria, involving gums, palate, inner surface of cheeks, lower surface of tongue and floor of mouth, etc. The base of these superficial ulcerations is either exposed and then greyish white, due to the necrosis of the tissues; or it is covered with thick brownish crusts. The condition is so characteristic that one might speak of it as a "stomatitis uraemica." These lesions are usually directly due to streptococcus infection of the weakened tissues.

In the majority of the chronic cases the systolic blood pressure was distinctly elevated, varying from 160 to 250. Elevations to 200 and more were present in five cases (17, 18, 22, 23, 26). As the cases are arranged somewhat according to the severity of the lesions in the kidneys, it is evident from the figures that the amount of destruction of kidney tissue in itself does not control this phenomenon. In fact, there are more cases with low pressures and small hearts among the cases with the most extensive destruction of renal tissue than among those with less destruction. The patients with unusually high pressures were all rather strongly built males between 45 and 55. Three of them had a marked general arteriosclerosis, one had fairly normal, and the last one entirely normal arteries. On the other hand some of the cases with the most marked and extensive general arteriosclerosis had low pressures and small hearts. One gets the impression, therefore, that the pressure is forced up more energetically in comparatively vigorous individuals, when the disease develops comparatively rapidly and leads to death before extreme changes have taken place in the kidneys.

The cardiac hypertrophy is evidently caused by the hypertension, but it is by no means proportionate to it. The largest heart (24) was found in an individual with a blood pressure of 170, which on rest in bed came down to 135. On the whole, the hypertrophy of the heart remains within moderate limits, varying from one and one-fourth to one and one-half times normal size in bulk. The hypertrophy is primarily a concentric

hypertrophy of the left ventricle (see for instance cases 16 and 19), followed by its dilatation and later sometimes by involvement of the right heart; but the cases showing much dilatation on the right side and marked cyanotic atrophy of the liver, as a sign of chronic passive congestion in the peripheral veins, are quite small in number (see cases 19, 26, 27).

Cases with low pressures and normal, or even small, hearts are by no means rare, especially in very chronic cases with extreme contraction of the kidneys (see cases 25, 28, 29 and 32).

The relation of chronic nephritis to gout is again brought out prominently by our series of cases. Only one of them (30) had a definite clinical history of gouty arthritis, but gouty lesions in kidneys and elsewhere were encountered in five cases (24, 26, 27, 29, 30), without a systematic search in every instance. It is reasonable to assume, therefore, that actually the incidence was greater than is indicated in our records. It appears especially to occur in the very chronic cases with extreme kidney lesions (second half of this series). The recent observations of Denis[5] that in healthy individuals an excess of purins is rapidly excreted, leaving the uric acid percentage in the blood undisturbed, whereas retention follows early in cases with renal insufficiency, may furnish some clue to the frequency of this association.

The death of the patients was either the result of terminal infection, usually broncho-pneumonia (cases 16, 23, 24, 25, 27, 28, 29, 30), or of true uraemia (17, 18, 19, 20, 21, 22, 26, 27, 28, 31). In the latter case the patients often developed uraemic coma, but some showed no disturbance of consciousness, merely excessive dyspnoea (19, 20, 28).

As may be seen from the table of summary of the cases, the urinary findings were fairly constant in all cases. Polyuria was a very prominent symptom, occurring at one time or another in seven out of the thirteen cases in which anything definite is known of the urine. This was commonly associated with frequent urination at night (nycturia). The amount of urine was definitely increased in about one-half of the cases. In three the quantity is designated as decreased. The specific gravity was generally low (1010 and less). The lowest specific gravity (1002) was found in the most acute case (16) of this series. The specific gravity was low, not only in the cases with polyuria, but also in some of those with a decreased amount of urine, suggesting hyposthenuria (Schlayer). (See cases 22, 23 and 24.)

With few exceptions (19, 29, 30), the urine contained much albumin

[5] Denis, "The Effect of ingested Purins on the Uric Acid Content of the Blood," *Journ. of Biol. Chem.*, 1913, XXIII, 147

(at least a heavy cloud). The albuminuria was moderate in cases 19 and 29. In case 30 no albumin was found, but the patient was at the hospital for a short time and there is record of one examination only.

The finding of casts was not so constant. There were several cases in which no casts were found, but repeated examination usually revealed showers of casts once in a while. Frequent examinations of the urinary sediment are therefore of great importance. Leucocytes and erythrocytes were discovered only occasionally. The difficulty of finding formed elements in the urine at times is rather astonishing, because in sections of these kidneys casts are always fairly numerous, and frequently quite a few tubules are filled with blood or leucocytes (see protocols of individual cases). It may be that in these later stages the contents of the tubules are washed out less easily and are carried down only when there is a more or less sudden flood of urine.

The phenolsulphone-phthalein test was employed in a few cases only, many of them dating back before its introduction. In every instance the excretion was distinctly slowed. In case 26 there was no excretion in three trials.

The gross appearances of the kidneys varied considerably, except that they all showed evidences of contraction. The capsule was more or less thickened and adherent. The surface of the kidneys was either smooth or granular, or full of large irregular scars, more or less lobulated, according to the distribution of the newly formed connective tissue.[6] The color was frequently mottled, purple and grey, or in other cases dark red, in others again quite pale. In quite a few cases one could make out small petechial haemorrhages. The number of them varied from a few to a great many. In some instances the color of the organ was distinctly brown on account of an abundant deposit of haematogenous pigment in the epithelium. On the cut surface the cortex naturally appeared more or less contracted, and on account of the great structural alterations the normal markings of the cortex had disappeared to a great extent. If there was much epithelial degeneration, opaque, frequent yellowish spots were seen scattered through the cortex. The arteries on the cut surface varied greatly. In some cases they were distinctly thickened, in others they were entirely normal. The same is true of the main stems of the renal arteries.

Histologically the connecting link of all cases was the inflammatory lesions in the glomeruli and the inflammatory proliferation and eventual fibrosis of the connective tissue. The great variety of lesions encountered

[6] The differences are well shown in the photographs accompanying the individual cases. They are all taken at nearly one-half normal size.

is well illustrated in the photomicrographs. Still they all show the same pattern. The inflammatory character of these lesions is naturally most evident in the more acute cases, but even in the very old cases typical subacute lesions may be encountered in some of the glomeruli (see photomicrograph of case 31) and in certain parts of the interstitial tissue. Eventually most of the glomeruli become shrunken and fibrous. The newly formed connective tissue also becomes more and more fibrous and the neutrophilic leucocytes disappear from it, but eosinophiles and "Mastzellen" persist for a long time.

The extent of the epithelial degeneration varied very much. In some cases granular and fatty degeneration was very well marked, in others there was hardly any evidence of it. I cannot say that it appeared as if the cases with much epithelial degeneration were more likely to develop oedema, as has been suggested. It is to be considered that the relation of the oedema to the epithelial degeneration may be the opposite from that which is usually assumed. If there is general oedema at the time of death involving the kidneys, the existence of this oedema in the kidneys may very well favor the development of degenerative changes in the epithelium.

Eventually the majority of the tubules collapse, and the amount of tissue destruction may continue to an astonishing degree before death ensues. In those cases in which the glomerular involvement and the connective tissue development are of a patchy character the remaining comparatively normal glomeruli and tubules often show evidences of compensatory hypertrophy. These latter conditions, however, do not seem to have much effect on the clinical picture. The development of numerous small cysts is quite common in the later stages.

Bacteria were found in the tissues in one early case only (case 10). It was the most acute case of this series, a case in which there existed an infection of old atheromatous ulcers with diplostreptococci. The diplostreptococci were found in many capillaries, and a few outside in the inflamed connective tissue. Once more, no bacteria were discovered in the diseased glomeruli.

This same case had acute and very marked lesions in the arterioles, consisting of hyaline thrombosis which in some places filled the arterioles completely, in others formed a thick layer on the inner surface partly above, partly below the endothelium. In other small arteries these hyaline masses had been partly or completely organized, giving rise eventually to the picture of a cellular endarteritis. In what appeared as the later stages of the same process much elastic tissue had developed in the thickened intima, in such a way that eventually an appearance was pro-

duced resembling that described by Jores as characteristic of the "functional" hyperplasia of the intima in arteriosclerosis.

In case 18 the thrombotic obstruction of some of the arterioles had given rise to the formation of many microscopic anaemic necroses. Both the small and the larger arteries showed a very marked thickening of the intima, partly with hyperplastic development of the elastic tissue, partly without. Similarly the two processes were mixed in case 17. In case 20 the arterial changes seem to be old, both in arterioles and in the larger arteries, and we find much elastic tissue in both places. In case 22 some small arteries show "endarteritis," others "arteriosclerosis." In this and many other specimens (see individual records) one finds all transitional stages between these two conditions.

In a general way one may state that the arterioles in the kidney are affected in all cases, but that even in the oldest and most severe cases, like cases 31 and 32, the larger arteries in the kidneys and elsewhere may show very little evidence of disease.

It appears therefore ill advised to indulge in too much speculation in regard to the etiology of the process in the arteries from the histological appearance of the lesions, and I believe that until further proof to the contrary is forthcoming we are justified in assuming that the changes in the arteries in these diseased kidneys are of an inflammatory nature, just as the rest of the lesions. This interpretation would harmonize very well with the observation that in the small arteries at least the proliferation of the intima is frequently preceded by lateral thrombosis, bearing in mind the fact that inflammation of the arterial wall necessarily would favor thrombosis.

In conclusion I may be permitted to add a few general statements. It may seem as if this were hardly warranted on account of the small number of cases studied; and there certainly would be justification for criticism, if an attempt were made to elaborate a complete pathology and symptomatology of chronic nephritis on such a slender basis. On this account all preceding statements have been worded so as to refer to the individual cases only. But, on the other hand, a few thoroughly studied cases may give some food for general reflection.

If these cases teach anything, they certainly bring out very clearly the loose association which exists between the condition in the kidneys and a number of other phenomena which have usually been rather loosely described as "nephritic." Terms like "nephritic" oedema or "nephritic" hypertension cannot fail to give the impression that the oedema or the

hypertension depend directly on the condition of the kidneys. To my mind nothing could be further from the truth. These conditions are frequently associated with nephritis, but the kidneys themselves play no demonstrable rôle in their origin.

This will be perhaps more easily conceded in case of the oedema. All attempts at explaining the oedema on the basis of the disease in the kidneys have failed, and as a matter of fact a cursory study of these thirty-two cases will show that there is no one element in the pathology of the kidneys with which the oedema could be connected. Practically the same lesions may be observed in the kidneys of patients which were "water-logged" long and often, and in patients who had oedema rarely or not at all. One may object that the anatomical picture of the kidney does not give a true representation of its functional capacity, and that functional tests show that certain *functional* derangements of the kidney are apt to be associated with oedema. I very much hesitate to express an opinion on this latter point on account of lack of experience and knowledge; but this much is certain, that in these functional studies it is often difficult to determine what is cause and effect; and there is certainly no unanimity of opinion among those most competent to judge in questions of this character. But apart from all such controversies, how much easier of solution does the whole question become if we give up this idea and state the relation somewhat in the following manner: The agency which produces the nephritis (certain bacterial toxins), in addition to injuring the capillaries in the kidneys also injures them elsewhere, and this produces the oedema.

We need only to think of the word "inflammation" to realize that this is possible, because the most striking effect of bacterial toxins in the tissues is injury to the capillaries. Of diffuse injury to the renal capillaries (besides the characteristic lesions in the glomeruli), we have ample evidence in the acute and subacute cases of the disease. The oedematous swelling of the kidneys is often extreme, and the extent and importance of this oedema seems to have hardly sufficiently impressed itself upon anatomists and clinicians. If this is the true relation of things, we can understand much more easily why the relation of the nephritis to the oedema should be so varying. In a certain case the kidneys may be damaged very severely, but the capillaries in it or elsewhere much less so; and vice versa. Given damaged capillaries, the factors which damage them additionally or which in other ways favor the development of oedema may naturally provoke to manifestation a condition which may be more or less latent, or aggravate an oedema that is already plainly in existence. The damage being general, the

capillaries in the delicate structure of the eye-lids may show the damage first; whereas in other cases the oedema may first show in places where the circulation is relatively poor, as in the region of the ankles.

It appears to me that an assumption like the one made above clears away innumerable difficulties, and at the same time permits the utilization of all the important data which have gradually accumulated as a result of patient clinical investigation. I should suggest, therefore, that the term "nephritic oedema" should be replaced by "oedema in nephritis."

The same way with "nephritic" hypertension. Here also the looseness of the interrelation of this phenomenon to the disease of the kidneys is so evident that it does not need special emphasis; in fact, this lack of correlation has been the despair of all those who have attempted its explanation scientifically. It appears a little more hazardous to ascribe these differences also to differences in the action of the causative agent which provokes the nephritis. It is not known of bacterial toxins that they affect the tonus of the arterioles, and yet, whatever causes the hypertension must affect them. The condition of the large arteries is immaterial. An increased activity of the heart would be easily compensated for by the vasomotor regulatory mechanism; but when the tonus of the arterioles is increased the vasomotor regulation breaks down, as we know in the case of adrenalin and pituitrin hypertension, probably because the mechanism works by means of the arterioles and has little reflex control over the heart action. If it could be shown that substances produced by bacteria directly or indirectly had a pressor action, then all difficulties would disappear, as in the similar case of the oedema. Then one would be able to understand why we should have sometimes early and extreme hypertension, at other times none at all. If we make the further assumption that these or similar substances *sometimes* do not only stimulate the arterial wall to contraction, but also injure it, we would come much nearer to the solution of the "arteriosclerosis" problem; in fact it might lead us to an entirely new conception of the etiology of arteriosclerosis and its puzzling relation to hypertension and nephritis, because after all is said and done arteriosclerosis and arteriosclerotic hypertension have some intimate relation to nephritis, but certainly not the one usually thought of, namely, that the nephritis is the primary factor. An assumption like the one mentioned above is naturally still altogether speculative, and it will take much work to get close enough to these important problems to make positive statements; but, whatever the relation is, I believe it may be positively asserted that nephritis and hypertension are not related to one another as cause and effect.

Clinicians have already recognized that certain forms of uraemia

are not due to the injury to kidney tissue, but to other factors. The convulsive form of uraemia is, for instance, almost certainly due to disturbances in the cranial cavity, the exact nature of which is still far from being recognized; and similarly it may be with other forms of this protean symptom-complex. The only condition in which we have good reason to believe that it is directly the consequence of destruction of kidney tissue is what clinicians now usually speak of as "true" uraemia; and in this condition the evidence that it is due to an inefficiency on the part of the kidneys to excrete some as yet unknown substance or substances has been accumulating rapidly in the last years.

In regard to the changes in the *composition* of the urine and its sediment I wish to emphasize once more, as has been done often enough before that the condition of the urine is a fairly accurate measure of the severity of the disease in the kidneys at a given time, and no measure at all of the extent of the damage to the renal tissue. Polyuria and hyposthenuria more particularly point to serious involvement of much kidney tissue, although of course other possible factors have to be taken into account. The records also bring out clearly that frequent careful urinanalyses are of great importance in the clinical recognition of the disease.

It is impossible to condense the result of these observations into a few phrases, but our main conclusions might be formulated as follows:

1. Diffuse glomerulo-nephritis is a disease which may occur in acute, subacute, or chronic form.

2. The etiology of the acute and subacute forms is evidently to be found in bacterial infection, and this is quite probably true of the chronic form.

3. The bacteria concerned are commonly, but not necessarily, members of the streptococcus family.

4. It is probable that the continuance of the disease in the kidneys is due to the continuance of the infection in some often more or less hidden focus.

5. It is suggested that one should look upon the oedema, the hypertension, the arteriosclerosis, and certain uraemic manifestations merely as being frequently associated with nephritis, rather than as being directly dependent upon it.

6. It is quite conceivable that these manifestations are the result of the fortuitous action upon other tissues of the same cause which injures the kidneys.

RECORD OF CASES

Case 1. Old focal and acute diffuse glomerulo-nephritis in man of 52 years, with chronic diplostreptococcic endocarditis.

XVII, 60.— J. K., strongly built, emaciated American engineer, 52 years old.

The patient had had occasional attacks of sore throat. His first definite symptoms were observed eight years before death, when he developed palpitations with dyspnoea. A similar attack with chills and fever was observed three years later. Eight months before death he had oedema of the legs. His last attack began four months before his death with abdominal cramps, diarrhoea, dyspnoea, and expectoration. During this last attack he ran an irregular septic temperature. Clinically he showed evidences of aortic regurgitation. There was marked oedema of the legs and later of the trunk, and symptoms of hydrothorax. Towards the end oedema and hydrothorax disappeared. He had a slight anaemia (4,000,000 reds; Hb. 60%), no leucocytosis (3-10,000). He had a positive Wassermann reaction, although he denied lues and nothing suggestive of syphilis was found at autopsy. Two blood cultures were negative. Diplostreptococci were found in the urine. The urine showed a heavy cloud of albumin, many hyaline and granular casts. It was first decreased in amount, later increased with the disappearance of the oedema. The phenolsulphone-phthalein secretion was slowed (35% 1st hour, 15% the 2d).

Necropsy revealed an old, aortic diplostreptococcic endocarditis with regurgitation, and a large spleen with numerous large areas of haemorrhagic softening which were full of streptococci. There was a slight general arteriosclerosis.

The kidneys were slightly swollen (12 x 6 x 3 cm.) and smooth. The cortex was fairly wide, opaque, and showed a moderate number of haemorrhagic spots. There was a small anaemic infarction in the right kidney.

Sections showed few fibrous glomeruli with areas of cellular infiltration and moderate thickening of the connective tissue about them; few neutrophilic and eosinophilic leucocytes in these areas of cellular infiltration; infiltration of most glomeruli with neutrophilic leucocytes; recent hyaline necrosis of loops in a fair number; no extra-capillary

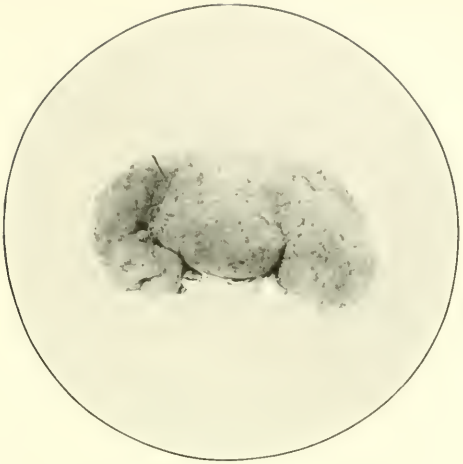

Fig. 1.

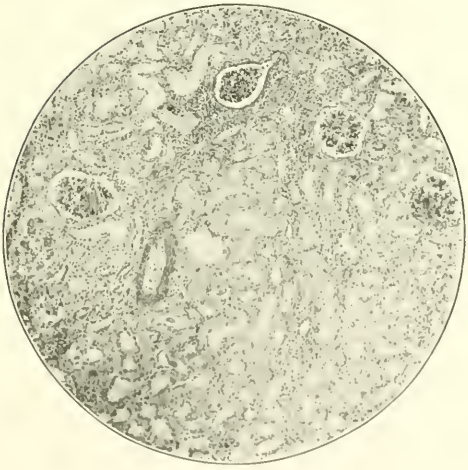

Fig. 2.

proliferation; very marked hyperaemia; few haemorrhages; few casts, little epithelial degeneration; beginning "arteriosclerosis" of some small arteries. Many small vessels were filled with coccus-emboli. The tissue about some of these was necrotic and showed beginning suppuration. No cocci were found in any of the diseased glomeruli.

Case 2. Old focal and acute diffuse glomerulo-nephritis in man of 54 years, following recrudescence of chronic diplostreptococcic endocarditis.

XVII, 31.—J. N., American kitchen-helper, 54 years of age.

Patient had an attack of acute polyarticular rheumatism followed by sharp precordial pain radiating into arms twenty years before death. Since then he had had three to four attacks a year. He was always

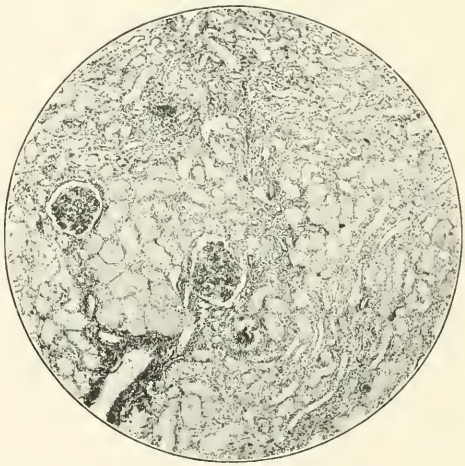

Fig. 3.

short of breath, and had palpitations of the heart. He was nervous and slept poorly. At times he had severe headaches, dizziness and night sweats. Lately he complained of renewed pain over the heart, shortness of breath, and oedema at the ankles which he observed for the first time. Clinically he presented evidences of aortic stenosis and regurgitation.

His blood pressure was 170 on entrance, but later went down to 140 150. He had a slight anaemia (4,000,000 reds; Hb. 85%) and a slight leucocytosis (10,000). He had a positive Wassermann reaction, although he denied lues; nothing suggestive of syphilis was found at autopsy. His temperature was at times subnormal, and his pulse rate varied between 80 and 100. His urine showed a light cloud of albumin and few granular casts.

Necropsy revealed an old aortic diplostreptococcic endocarditis with recent exacerbation, moderate general arteriosclerosis.

The kidneys were of about normal size and full of minute haemorrhages.

Sections showed few glomeruli with old glomerulo-nephritis and small areas of cellular infiltration and connective tissue proliferation in the vicinity; infiltration with neutrophilic leucocytes in majority of glomeruli; necrotic loops in few of them; extra-capillary proliferation about some of these tufts; many haemorrhages, few leucocytes, few casts in tubules; marked leucocytosis in capillaries and few neutrophilic leucocytes in the interstitial tissue; marked fatty degeneration and beginning necrosis of the epithelium; beginning "arteriosclerosis" in some small arteries. No pathogenic bacteria were found in the sections

Case 3. Old focal and acute diffuse glomerulo-nephritis in a man of 41 years, with old diplostreptococcic endocarditis.

XVII, 188.—M. E., fairly strongly built, fairly well nourished Spanish farmhand and teamster, 41 years of age.

History imperfect on account of condition of patient, who died one day after entrance. He claimed to have been well until a sudden breakdown three weeks before, while at work in the fields. Since then he became weaker, dyspnoeic and oedematous. At first he had frequent urination of small amounts of urine; later he had to urinate less frequently, and the oedematous swelling increased correspondingly. A few days before death he began to have bloody expectoration. Clinical examination showed extreme dyspnoea, much cough with bloody expectoration, a heart of apparently normal size, a blowing systolic murmur, much oedema. He had a high pulse rate (103) and a moderate temperature 101 F). His blood-pressure was 140. His urine had a specific gravity of 1012, contained much albumin, many hyaline and granular casts, and few leucocytes.

Necropsy revealed an old aortic diplostreptococcic endocarditis with some stenosis, a heart about one and one-fourth times normal size, cyan

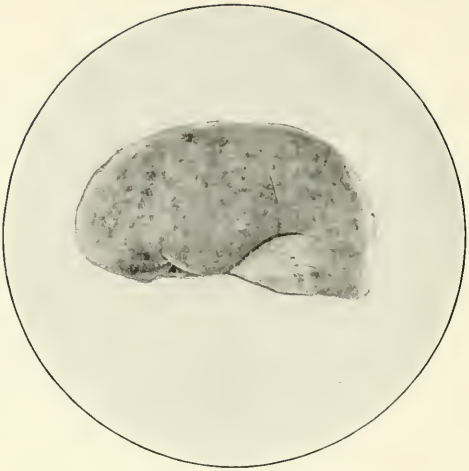

Fig. 4.

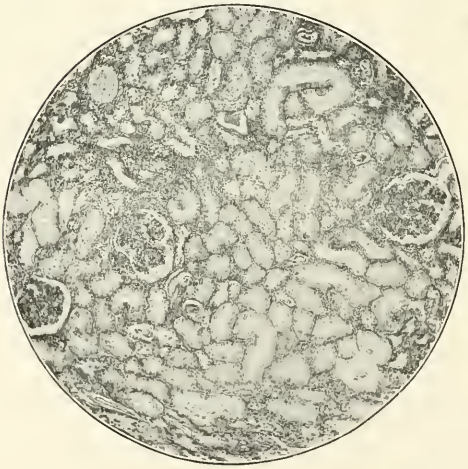

Fig. 5.

otic atrophy of liver, much oedema, ascites and hydrothorax, also an acute glaucoma of the left eye. The arteries were practically normal.

The kidneys were swollen (13 x 7 x 4½ cm.) and smooth. The cortex was wide, yellow, opaque, and full of minute haemorrhages. There was an old infarct in the left kidney.

Sections showed old glomerulo-nephritis in few glomeruli, which were surrounded by small areas of cellular infiltration, and fibrous thickening of the connective tissue. The majority of the glomeruli were infiltrated with neutrophilic leucocytes; hyaline necroses were found in several, and beginning extra-capillary proliferation in some. Some tubules were filled with blood; many also contained leucocytes. The interstitial tissue was moderately infiltrated with neutrophiles. There was little degeneration in the epithelium; beginning "arteriosclerosis" in few small arteries. The sections were too badly contaminated to permit of bacteriological examination.

Case 4. Acute glomerulo-nephritis in woman of 33 years, with cirrhosis and large septic phagedenic ulcers of leg.

XVIII, 158.—Mrs. A. B., delicately built, fairly well nourished Italian housewife, 33 years of age.

Patient came to clinic two years before death, complaining of swelling of abdomen and feet. Five years before death she had her first attack of swelling of the abdomen with jaundice. About three months before death ulcers developed on the right leg, which became progressively worse. One month before death the symptoms of cirrhosis became more aggravated. Clinical examination showed the usual symptoms of cirrhosis, large phagedenic ulcers on right leg. Treatment with salvarsan made the ulcers on the legs much worse. Her temperature was high and somewhat irregular; her pulse accelerated and irregular. Towards the end she became irrational, and some oedema appeared on her face. The Wassermann reaction, which had been negative before, became positive at this time. She was quite anaemic (Hb. 63%). The urine contained much albumin, at times many granular and cellular casts, and very many leucocytes.

Necropsy revealed extensive old cirrhosis and several large phagedenic ulcers on right leg. Smears from the most acute one of these ulcers showed many streptococci. Streptococci were also found in a thrombus in the right auricle and in the spleen. The heart was slightly dilated on the right side. The large blood-vessels were normal.

The capsule of the kidneys stripped easily. The surface was very slightly granular. They were extremely hyperaemic and oedematous, and very distinctly swollen (12½ x 6 x 4½ cm.). On the cut surface the cortex was wide, and showed a certain number of small opaque spots. No haemorrhages were seen in the gross specimen.

Microscopic sections showed a diffuse intra-capillary, and in places extra-capillary, glomerulo-nephritis. The glomeruli were heavily in-

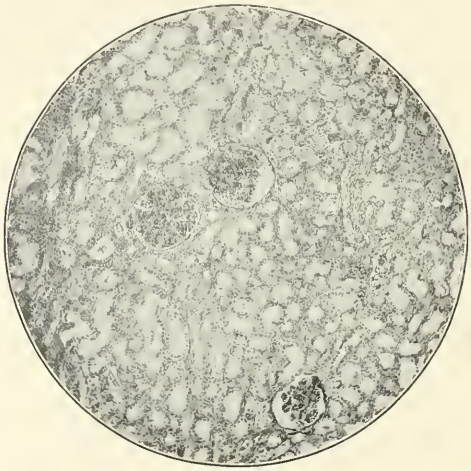

Fig. 6.

filtrated with polymorphonuclear leucocytes. Many of them showed hyaline necrosis of some of the loops. In few glomeruli the changes were advanced to the subacute stage. Many tubules were filled with blood and leucocytes. The epithelium showed some granular and a little fatty degeneration. The interstitial tissue was hyperaemic, oedematous, and slightly proliferated. There was a moderate infiltration, with granular leucocytes and lymphocytes. No bacteria were found in sections. The small arteries were normal, the larger ones were slightly "arterio-sclerotic."

Case 5. Early subacute glomerulo-nephritis in a woman of 33 years with subacute diplostreptococcic endocarditis.

XVIII. 166.—Mrs. R. B., strongly built, poorly nourished Italian housewife, 33 years of age.

Patient was admitted to hospital ten days before her death, complaining of vomiting, shortness of breath, and swelling of feet. Nine months before, she had an attack of acute polyarticular rheumatism, ushered in by tonsillitis. The pains in the joints continued intermit-

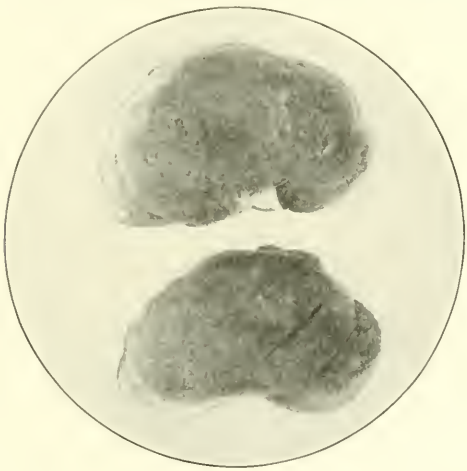

Fig. 7.

tently for about six months. Ten weeks before admission her stomach trouble began, and she vomited frequently. Her dyspnoea started six weeks later, and the oedema commenced one week before entrance. Clinical examination showed marked dyspnoea, slight icterus, coated tongue, an enlargement of the heart to the left, a systolic blowing murmur at the apex, transmitted to axilla and back, also a presystolic murmur, marked general cyanosis and oedema, petechial haemorrhages in skin and mucous membranes. The patient vomited very much, was very restless at times, at others drowsy, had some muscular twitchings in face, and died of gradual circulatory failure. She was distinctly anaemic (3,302,000 reds; 48% Hb.). There was some leucocytosis (12,740).

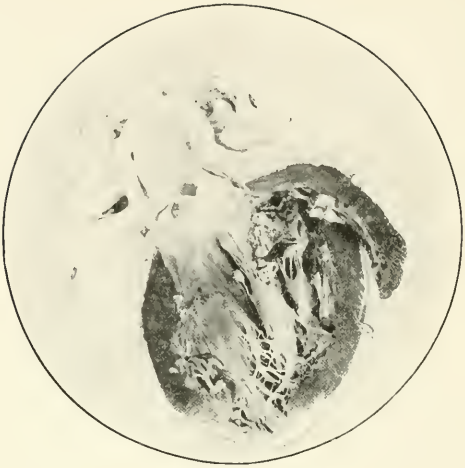

Fig. 8.

Fig. 9.

Diplostreptococci were obtained in blood culture. Her blood pressure was 100. The temperature was subnormal, with elevations to 99 F. The pulse rate varied between 80 and 100. The urine contained much albumin, many hyaline, granular and cellular casts, many leucocytes and much blood, also diplostreptococci.

Necropsy revealed subacute diplostreptococcic endocarditis of mitral and tricuspid valves, embolic septic foci in heart-muscle, infarcts in spleen and kidney, septic necroses in liver, cholelithiasis, and terminal broncho-pneumonia. The heart was moderately enlarged on the right side on account of mitral disease. The blood-vessels were normal.

The kidneys were swollen ($11\frac{1}{2} \times 6\frac{1}{2} \times 4$ cm.; $12 \times 7 \times 5$ respectively). The capsules stripped easily. The surface was smooth, dark greyish red, and studded with minute haemorrhages. On the cut surface the cortex was wide, distinctly oedematous, and greyish red.

Microscopic sections showed diffuse acute and subacute glomerulo-nephritis (intra- and extra-capillary); much blood and many leucocytes in tubules, many neutrophilic leucocytes in glomeruli and in interstitial tissue, few eosinophiles and basophiles, comparatively little epithelial degeneration, and beginning proliferation of the connective tissue; arteries normal. No bacteria were found in sections, in spite of careful search.

Case 6. Early subacute glomerulo-nephritis in an infant with congenital syphilis and suppurative colon-bacillus pyelitis.

XVI, 56.—A. C., anaemic female child, $1\frac{1}{2}$ months of age.

The child was apparently normal at birth, was sick for about two weeks with sanguino-purulent discharge from nose, and fever to 101 F. Several blisters developed on abdomen. At the hospital occurred a more general eruption of red blisters. The hands were oedematous on entrance, but the oedema disappeared later. Moist râles were heard over the lungs. The Wassermann reaction was positive. A heavy cloud of albumin was found in the urine, a few doubtful hyaline casts, and many leucocytes. Patient died in collapse with symptoms of pulmonary oedema.

Necropsy revealed syphilitic rhagades at mouth, syphilitic pneumonia and subacute septic pneumonia, syphilitic cirrhosis and miliary syphilomata of the liver, subacute deep ulcerative infection of renal pelvis with colon-bacilli and beginning involvement of kidneys. The arteries were normal.

The kidneys were large. The cortex was opaque and swollen.

Sections showed hyaline necrosis of vascular loops in the majority of the glomeruli, with subacute glomerulitis (extra-capillary). Many

tubules were filled with blood, others contained leucocytes. There was a marked infiltration of the interstitial tissue with neutrophilic, eosino-

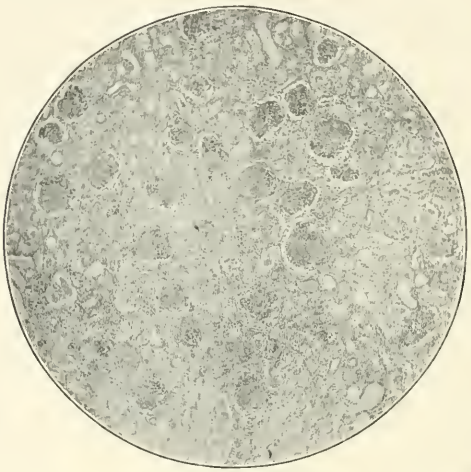

Fig. 10.

philic leucocytes and plasma cells, and cellular proliferation of the connective tissue. The vessels were normal. No bacteria were found in the sections, except at the evidently infected places.

Case 7. Subacute glomerulo-nephritis in a man of 40 years, following subacute endocarditis.

XVII, 163.— E. G., dishwasher, 40 years of age.

Patient had a paralytic stroke associated with left-sided hemiplegia and sensory aphasia seven months before death. He had a chancre two years before, and at the time he came to the hospital had a positive Wassermann reaction. Clinically he showed a systolic murmur at the apex, general oedema, some anaemia (4,800,000 reds, 85% Hb.), and slight leucocytosis (11,200). He had an irregular temperature varying between 96° and 102° F. His pulse rate varied between 70 and 100. His urine contained a moderate amount of albumin and a few hyaline casts.

Necropsy revealed a subacute diplostreptococcic endocarditis of the mitral valve, with regurgitation, an embolic softening in the region of

the right island of Reil, a beginning cyanotic atrophy of the liver, general oedema, marked hydrothorax and normal arteries.

The kidneys were swollen; the cortex was rather wide and opaque, and full of petechial haemorrhages.

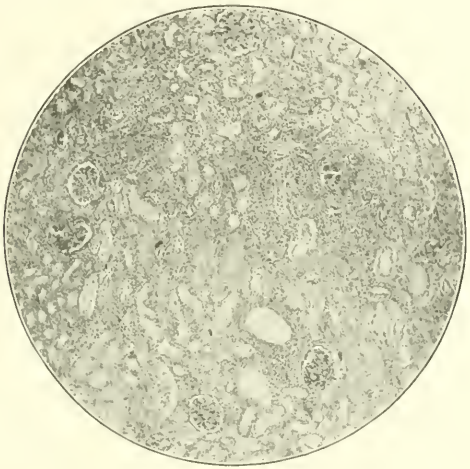

Fig. 11

Sections showed hyaline necroses in many glomeruli, typical diffuse subacute and more chronic glomerulo-nephritis (intra- and extra-capillary); moderate diffuse cellular thickening of the connective tissue, in which there were quite a few neutrophilic and less numerous eosinophilic and basophilic leucocytes; marked hyperaemia; blood and leucocytes in many tubules; much epithelial degeneration; normal blood vessels. No pathogenic bacteria were found in the sections.

Case 8. Marked subacute glomerulo-nephritis in a man of 45 years, following streptococcic infection of compound fracture.

XIV, 34. — J. W., strongly built, muscular American carpenter, 45 years old.

Patient had a compound fracture of the left leg eight and one-half months before death. The bones became united, but the wound never quite healed and later broke open, leaving a constantly discharging ulcer

from which a small piece of necrotic bone came away at one time. Many streptococci were found in the infected tissues. The temperature was normal most of the time, but there were sharp rises off and on. His

Fig. 12.

urine was smoky, contained much albumin, many hyaline and waxy casts, many red cells.

Necropsy revealed, in addition to the infected fracture, a marked anaemia and broncho-pneumonia, possibly a slight hypertrophy of the left ventricle, slight oedema of leg, slight general arteriosclerosis.

The kidneys were somewhat swollen (12 x 7 x 4 cm.). The surface was smooth, mottled grey and red. The cortex was wide, hyperaemic and oedematous, and full of minute haemorrhages.

Sections showed hyaline necrosis in vascular loops of many glomeruli; very characteristic acute and subacute glomerulo-nephritis (extracapillary) in practically all; moderate diffuse infiltration of interstitial tissue with neutrophiles, eosinophiles, basophiles, and marked diffuse fibrous thickening of the connective tissue. Many tubules were filled with blood, others with leucocytes. The epithelium showed much fatty degeneration. Slight "arteriosclerosis" in a few of the larger arteries. A few doubtful diplococci were found in the diseased glomeruli and in the leucocytes in some of the tubules.

Case 9. Subacute glomerulo-nephritis in a man of 33 years, following subacute diplostreptococcic endocarditis.

XV. 135.— H. D., strongly built, emaciated, American hospital orderly, 33 years of age.

Patient infected his finger eight months before his death. The infection was followed by chills and fever, increasing weakness, and gradual development of symptoms of septic endocarditis, with remittent fever and progressive anaemia (eventually 3,800,000 reds; 56% Hb., 5,000 leucocytes, and occasional myelocytes). Three months before his death

Fig. 13.

patient noticed oedema at ankles, increased thirst, and increased urination. Since this time he complained of headaches and dyspnoea. The Wassermann reaction was negative. Blood cultures were negative on two occasions. His urine was increased in quantity (specific gravity 1010-1016), showing a heavy cloud of albumin (about 0.5%), many hyaline and granular casts, a moderate number of leucocytes, and at times many red cells. Phenolsulphone-phthalein excretion two weeks before death: 40% in two hours.

Necropsy revealed a subacute aortic diplostreptococcic endocarditis with moderate stenosis and some insufficiency, a purulent mediastinitis,

and a fibrinous pleurisy, both due to the diplostreptococci, a large spleen with a septic infarction, no oedema, normal arteries.

The kidneys were of about normal size; the surface was smooth. The cortex was wide, opaque, intensely hyperaemic, and full of haemorrhages.

Sections showed hyaline necrosis of loops in many glomeruli, very typical subacute glomerulo-nephritis (intra-capillary) in practically all, large areas of cellular infiltration (containing neutrophilic leucocytes), and much fibrous thickening of the connective tissue, with beginning atrophy of the tubules. Some tubules were full of blood, others contained casts. Much granular and fatty degeneration was found in the epithelium, also extensive necrosis. Normal blood-vessels. No pathogenic bacteria were found in sections.

Case 10. Subacute glomerulo-nephritis with continued hypertension and cardiac oedema in woman of 27 years, following abscess of jaw.

XVIII, 106.—M. O. A., poorly nourished Spanish housewife, 27 years old.

Twenty-one months before death, patient had considerable trouble with her teeth, lasting for eight months; finally alveolar abscess developed, and one tooth had to be removed. This abscess involved lower jaw, and had to be drained from outside. She had been apparently well since then, until four weeks before her death, when she developed a painless oedema of the legs, without any other symptoms. The swelling continued, and the abdomen also became involved. Ten days before death, symptoms of an acute infection developed in the right leg. She developed an irregular fever to 102° F; her pulse rate varied between 100 and 140. There was also some leucocytosis (10-15,000). Clinically there were no important findings except oedema and evidences of cellulitis. Her haemoglobin was 80%, her blood pressure 160, gradually rising to 170. Her urine was quite scanty, specific gravity 1010; it contained much albumin, many hyaline and granular casts, many red and white cells. She had no symptoms of uraemia, and died of the acute streptococcic infection of her leg.

Necropsy revealed streptococcic cellulitis of the right leg, bronchopneumonia, some ascites (a pint of fluid), and an acute cystitis. Her left ventricle was slightly hypertrophied. There was no arteriosclerosis except in the renal arteries, where it was of a moderate degree.

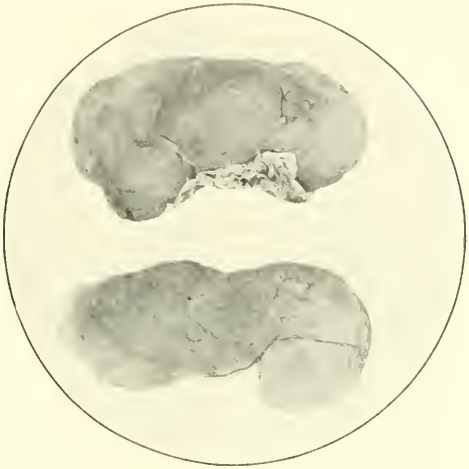

Fig. 14.

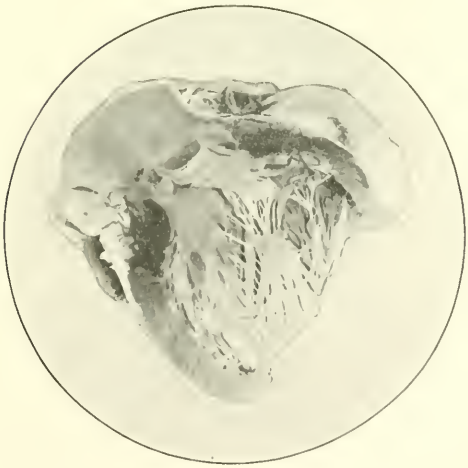

Fig. 15.

Her kidneys were of about normal size (12 x 5 x 4 cm.); the capsule was slightly adherent; the surface slightly roughened. The cortex was rather wide, yellow, and opaque.

Microscopical sections showed subacute, peri-capillary glomerulonephritis in many glomeruli, with development of fibrous connective tissue between capillaries, hyaline degeneration of the wall of some of the

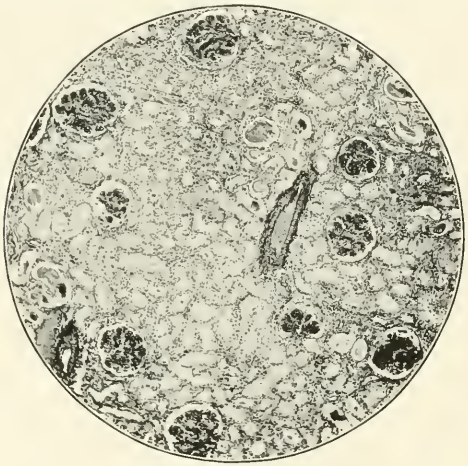

Fig. 16.

capillaries in the tufts, moderate diffuse thickening of the connective tissue with beginning atrophy of some of the tubules, leucocytes in many tubules, many hyaline casts, no haemorrhages, and much epithelial degeneration. The thickened interstitial tissue is almost altogether fibrous. There are very few small areas of lymphocytic infiltration; no granular leucocytes were found in the tissues. No bacteria were found in the sections, in spite of continued search.

Case 11. Late subacute glomerulo-nephritis in a man of 51 years, following chronic diplostreptococcic endocarditis.

XVII, 110.— M. A., well nourished Norwegian male cook, 51 years of age.

Patient began to complain of heart trouble four years before his death. He had had some oedema. He came to the hospital about six

weeks before death, complaining of vomiting and dyspnoea. Clinically, he showed evidence of an enlargement of the heart, and a marked diastolic murmur, also symptoms of aortic aneurysm. The backgrounds of his eyes were normal; there was no definite evidence of uraemia. His temperature was subnormal and slightly irregular. His pulse rate varied between 90 and 100. His blood showed a secondary anaemia (3,312,000 reds, 60% Hb.) and a leucopenia (6200). He had a syphilitic history and a positive Wassermann reaction. His blood pressure, gradually

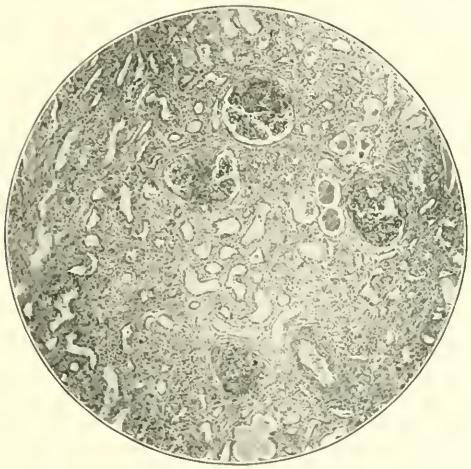

Fig. 17.

rising, varied from 180 to 220. Since over one-half year before death, he had noticed polyuria up to one gallon a day. The polyuria continued while he was at the hospital. His urine contained much albumin, many epithelial and granular casts, a few leucocytes, occasionally many red cells. It had a low specific gravity (1005-1010). There was practically no elimination of phenolsulphone-phthalein in three successive tests.

Necropsy revealed syphilis of the aorta and an aneurysm of the arch; a chronic diplostreptococcic endocarditis on the ventricular side of the large sail of the mitral valve and of the aortic valves with little deformity of the aortic cusps, and acute diplostreptococcic pericarditis, slight ascites, and moderate hydrothorax; old cyanotic atrophy of liver be-

ginning amyloid degeneration of the spleen, no amyloid in the kidneys. The heart was twice normal size, with a very marked hypertrophy of the left ventricle. The renal and splenic arteries were markedly sclerotic.

The kidneys were slightly enlarged (13 x 7 x 4 cm.), the surface was somewhat rough, dark red, and full of haemorrhages. On the cut surface the cortex appeared slightly reduced and opaque.

Sections showed very marked diffuse, chronic, subacute and acute glomerulo-nephritis (intra- and peri-capillary), with hyaline necrosis of many vascular loops, fibrin in capsules of many glomeruli, much infiltration with granular leucocytes, especially with eosinophiles, and marked diffuse thickening of the connective tissue with atrophy of many tubules; blood, leucocytes, and casts in tubules; much granular degeneration and necrosis of the epithelium; slight "arteriosclerosis" of a few of the small arteries and several of the larger ones. No bacteria were found in sections.

Case 12. Late subacute glomerulo-nephritis in woman of 26 years with repeated attacks of tonsillitis, a general diplostreptococcic sepsis with infection of the urinary tract, multiple thrombotic arterial obstruction.

XVIII, 61.— E. M., frail and extremely emaciated Irish-American housewife, 26 years of age.

Patient had numerous attacks of tonsillitis from infancy to four years before death. She was treated six years before death for nephritis following miscarriage. For the last five years she had much headache, associated with vomiting. Occasionally she had slight oedema of feet and ankles. Four months before death she complained of marked weakness, headaches associated with vomiting, pains in shoulders and arms, loss of power in left arm. She bled easily from her mucous membranes. Left foot had been cyanotic in region of big toe during cold spells for the past two years; she also had attacks of syncope in her fingers. Her eyesight began to fail at this time. When she entered the hospital a month before death, the toes of the left foot were cold and blue and her left arm contracted and atrophied. Later she developed dry gangrene of the left foot. Her tongue was dry and red, her breath uraemic. The heart action was heaving. There was a slight systolic and diastolic murmur, and considerable ascites. She later developed some oedema of the legs. Towards the end there was marked puffiness of the face. She had been complaining of failing eyesight for some time, and ophthalmoscopic examination revealed retinitis albuminurica. Shortly before her death,

she had profuse haemorrhages from the rectum. She died in uraemic coma. Her temperature was irregular, showing alternating periods of slight rises to 100° F. and of subnormal temperature. Her pulse rate was very irregular, varying between 80 and 130. She was very anaemic (Hb. 50%, 3,000,000 reds). Her leucocytes were normal except for a terminal leucocytosis. In a blood culture a pure growth of diplostreptococci was obtained; similar organisms were found in her urine. She denied all venereal infection, and had a negative Wassermann reaction. Her blood pressure was 105 on entrance, went up to 185, and then gradually down to 140. She had had nycturia[7] for the last ten years. Her urine was of about normal amount, of low specific gravity (1004-1008). It contained much albumin, sometimes few, at other times many casts of various kinds, some red blood corpuscles and leucocytes. Towards the end there was much pus in the urine. The phenolsulphone-phthalein secretion was much delayed (12% in two hours).

Fig. 18.

Necropsy revealed slight oedema of hands and legs, marked ascites. The appendix was surrounded by old adhesions. There was also some

[7] Urination at night.

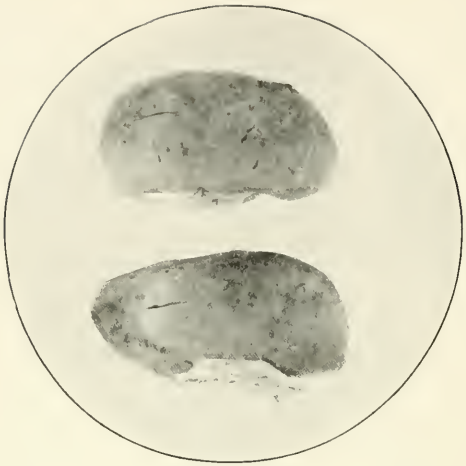

Fig. 19.

Fig. 20.

peritoneal thickening in the upper part of the abdominal cavity. The liver showed an old cyanotic atrophy. A large, deep, recent ulceration evidently due to arterial obstruction was found in the sigmoid flexure. The heart was of normal size; the left ventricle firm, full of small irregular necrotic spots, due to obstruction of small arteries. There were a few small yellow spots in the aorta. The renal pelves were slightly dilated. They contained a few drops of pus in which there were some diplostreptococci. The bladder also was infected with diplostreptococci. The left arm was contracted, and there was a dry gangrene of the left foot.

The left kidney was of about normal size (10½ × 4½ × 3 cm.), the right kidney smaller. The surface was mottled grey and red, and studded with petechial haemorrhages. The renal tissue was distinctly indurated, and the cortex narrowed to about 3 mm. Unfortunately an examination of the brain and of the peripheral arteries, and a thorough search for an old septic focus, was impossible.

Sections showed marked diffuse, subacute, and chronic glomerulonephritis (intra-capillary form), moderate cellular infiltration, and marked diffuse fibrous thickening of the connective tissue with atrophy of many tubules; much epithelial degeneration and many casts; blood and pus in the tubules, thrombotic hyaline deposits along inside of walls of many arterioles, anaemic necroses in pyramids due to thrombosis of small arteries. Other small arteries showed marked "endarteritis," and all the larger ones moderate "arteriosclerosis." No bacteria were found in sections.

Case 13. Subacute and chronic glomerulo-nephritis in a child of 8 years following infectious aneurysm of aorta.

XVI, 190.— V. P., female child, 8 years of age.

The patient had had measles, pertussis, mumps, and chickenpox. There was no history of sore throat, rheumatism, or scarlet fever. She was apparently perfectly well until about five months before death, when she began to have severe continuous headaches in the frontal region with much vomiting. About three weeks later she had a "spasm" lasting an hour and a half, with tongue bite and twitching of muscles of eyes and face. This was repeated six days later, and again after a few weeks. After the spasms she was unable to see well. The vomiting continued, and she developed increased thirst and polyuria. The patient lost much weight.

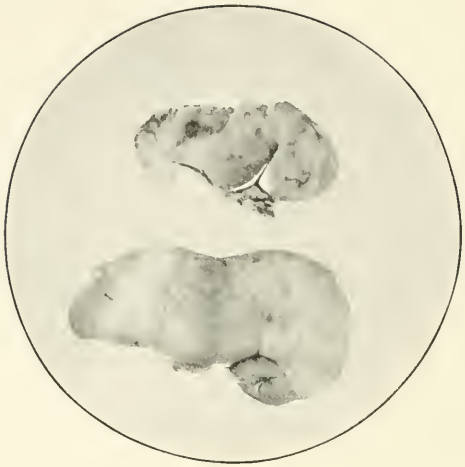

Fig. 21.

Fig. 22.

Clinical examination three months before death showed neuritis in left eye, enlargement of the heart with loud systolic murmur, painful enlargement of liver, no oedema. Later a papular eruption appeared on the extensor surfaces of extremities and on body. A retinal detachment developed in the left eye. At one time puffiness of the face was noticed. She complained of much pain in the pit of the stomach; nausea and vomiting continued intermittently. She suffered much from dyspnoea, and occasionally had pain in the region of the heart. Signs developed

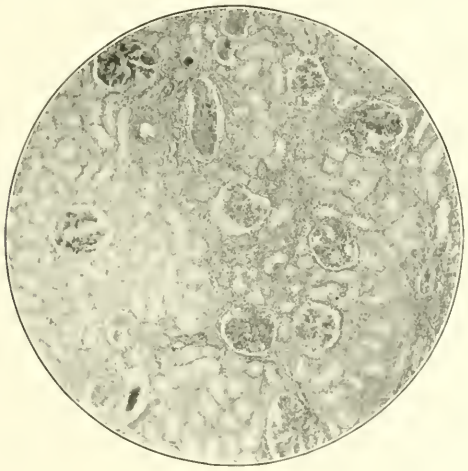

Fig. 23

of the presence of fluid in the pleural cavities. She had much cough, with blood-tinged sputum. Two months before death, the arteries in both eyes were found *much contracted*, and there was marked optic neuritis and retinitis in both eyes. Her temperature was slightly elevated and irregular. The Wassermann reaction was negative. There was a marked anaemia (Hb. 60%) and some leucocytosis (28,000 gradually decreasing to 10-12,000). The blood pressure was about 140. She had a very marked polyuria all the time; the urine was of low specific gravity (1002-1005). It contained little albumin and few hyaline casts, some leucocytes.

Necropsy revealed an infectious (diplostreptococcic) aneurysm of the upper abdominal aorta, involving the orifice of the left renal artery, which was entirely occluded; infarcts in lungs and spleen; and an old tuberculous focus in the left peribronchial lymph-glands. The heart showed normal valves. It was considerably enlarged, about twice normal size, with marked hypertrophy of the left and dilatation of the right ventricle. The left forearm and hand were oedematous on account of thrombosis of the subclavian vein. There was much chyloid fluid in both pleurae. The arterioles in the spleen were greatly thickened and hyaline. The other arteries were normal.

The left kidney was quite small (8 x 4 x 3½ cm.) with flat purple scars at upper pole and along the convexity. The right kidney was considerably swollen (12 x 5 x 4½ cm.); the cortex was wide, yellow, and opaque.

Sections of the left kidney showed old focal glomerulo-nephritis with numerous scars, no recent processes. Sections of the right kidney showed old glomerulo-nephritis in few glomeruli with scar formation near them; hyaline necrosis and subacute glomerulo-nephritis (intracapillary) in many glomeruli; slight infiltration of interstitial tissue with neutrophilic, eosinophilic, and basophilic leucocytes; considerable proliferation of the connective tissue; much granular degeneration of the epithelium; many casts, and leucocytes in some tubules. The blood-vessels were normal. No pathogenic bacteria were found in sections.

Case 14. Chronic glomerulo-nephritis in a child of 10 years with a history of repeated attacks of tonsillitis.

XVIII, 17.—A. B., poorly developed female child, 10 years of age.

The child had smallpox at an early age and had frequent attacks of tonsillitis. For the last two years she had had attacks of precordial pain, shortness of breath, and vomiting. She had been gradually running down with periods of exacerbation and remissions. She had had transient joint pains at times. Severe disturbance of compensation commenced about two weeks before death with oedema involving the face. Clinical examination one week before death showed a poorly developed, poorly nourished child with very marked dyspnoea, some oedema of the face but none elsewhere, heavily coated tongue, marked enlargement of heart; rapid, regular pulse (gallop rhythm), no murmurs, enlargement and tenderness of liver. A petechial rash appeared on the skin about one week before death. Towards the end she was semi-comatose, very restless (uraemia). There was some anaemia (3,606,000 reds,

Fig. 24

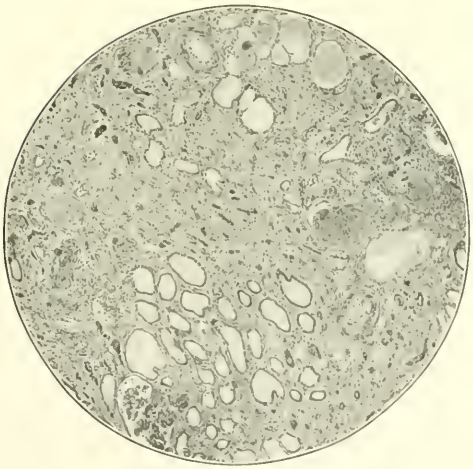

Fig. 25.

Hb. 80%) and a slight leucocytosis (11,400). The temperature was subnormal (about 96° F.) with rises to 99° and 100° F. The Wassermann reaction was negative. The urine (quantity could not be determined) showed a specific gravity of about 1010, a heavy cloud of albumin, several hyaline casts, and a few red cells. The blood pressure was 160 on entrance, but later fell to about 145.

Necropsy revealed a recent purulent diplostreptococcic vulvitis, a congenital fold at the lower end of the left ureter with slight hydronephrosis, ascites, hydrothorax, and slight oedema of the legs. The heart was at least twice normal size, with marked hypertrophy of the left ventricle. Except for a few small yellow spots in the abdominal aorta, the arteries were normal.

The kidneys had firmly adherent capsules. They were small (left 6 x 3 x 2 cm., right 9 x 4 x 3 cm.), finely granular, and the cortex was distinctly narrowed.

Sections showed very extensive involvement of glomeruli; some showed recent hyaline necrosis of loops, others typical subacute and chronic glomerulo-nephritis (intra-capillary). There was a marked diffuse thickening of the interstitial tissue, with heavy infiltration with neutrophilic, eosinophilic, and basophilic leucocytes; large areas of cicatrization; blood and leucocytes in few tubules; many casts, much epithelial degeneration; marked "endarteritis" in the small, and moderate "arteriosclerosis" in the large arteries. No pathogenic bacteria were found in sections.

Case 15. Chronic glomerulo-nephritis in boy of 6 years following streptococcic infection of urinary tract in nephrolithiasis.

XV. 120.— E. R., emaciated anaemic boy, 6 years of age.

Two years before the patient's death, a large stone was removed from the bladder. The urine at that time contained pus. The heart was clinically normal. Five months later evidences of cardiac hypertrophy developed. Later he had a right facial palsy. He had to urinate very frequently. The boy gradually went down-hill, and eventually died in uraemic coma. The history is incomplete, and there is no record of urinary analysis.

Necropsy revealed a small stone (1½ cm. in diameter) in right renal pelvis, with streptococcic infection of the urinary tract. The heart was somewhat enlarged, with definite hypertrophy of the left ventricle. Except for a few yellow spots in the aorta and in the coronaries, his arteries were normal.

Fig. 26.

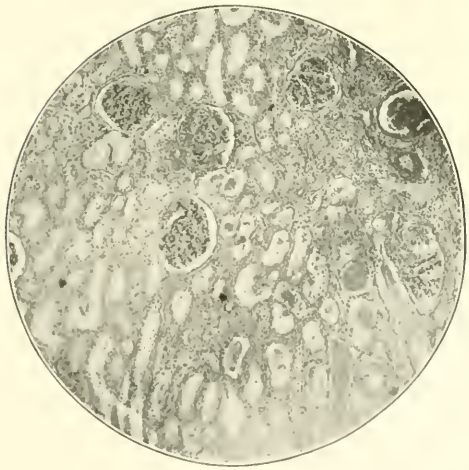

Fig. 27.

The left kidney showed many superficial purple scars, with narrowing of cortex. In other places the cortex was wide and opaque. The right kidney showed much more extensive cicatrization, with small nodules of fairly normal kidney tissue.

Sections showed very extensive chronic glomerulo-nephritis, with complete fibrosis of the glomeruli; large areas of cellular infiltration, and

Fig. 28.

fibrosis, with atrophy of tubules; many hyaline casts in the atrophic tubules. In the comparatively normal parts much recent and subacute glomerulo-nephritis (intra-capillary); and a few granular leucocytes in the tissues. Blood and leucocytes were found in some tubules. Much granular degeneration and necrosis of the epithelium. Hyaline thrombosis along wall in some small arteries. Very marked "endarteritis" in small and larger arteries, especially in the fibrous areas. The sections were too badly contaminated to permit of a bacteriological examination.

Case 16. Chronic glomerulo-nephritis in man of 53 years with diplostreptococcic sepsis (infected atheromatous ulcers in aorta).

XVIII. 70.—M. K., strongly built, fairly well nourished Japanese laundryman, 53 years of age.

(The history is imperfect, because the patient did not speak English, and was observed for a few days only.)

Patient had beri-beri at the age of 33. He was a heavy smoker, and he used much alcohol. For about the last three years his face and feet would become swollen at intervals, especially when he drank heavily, and at these times he complained of distress and of difficulty in breathing. His present attack started seventeen days before his death, with oedema. Later he developed a white membrane in the throat, which first appeared on his tonsils, spreading over the uvula and inside of the cheek. He developed a high fever, and had a very foul breath. Clinical examination showed puffiness of face, slight oedema of legs, angina and stomatitis, an apparently normal heart. The pulse was small, regular, rhythmical, and of low tension. The patient died with the signs of pulmonary oedema. His urine a few days before his death was of a very low specific gravity (1002), contained much albumin, occasional granular casts, and many white and red blood corpuscles.

Necropsy revealed slight oedema of conjunctivae and of cheeks, septic angina and stomatitis (diplostreptococcus infection). In the lower thoracic and in the abdominal aorta there were large atheromatous plaques, many of them ulcerated. In smears from these ulcers many diplostreptococci were found. There was an old thrombosis of the left iliac artery. The other arteries were somewhat dilated, otherwise normal. The spleen was of normal size, and contained many diplostreptococci. The arterioles in the spleen were distinctly thickened. The liver showed an incipient cyanotic atrophy. There were 500 cc. of fluid in the abdomen. The patient died of broncho-pneumonia and beginning pleurisy.

The heart was enlarged (one and one-half times normal size). The wall of the left ventricle was greatly thickened (16 mm. in diameter).[8] The heart muscle showed a marked fatty degeneration.

The kidneys were of about normal size (11 x 6 x 5 cm.), with granular surface. The tissue was greyish, with red blotches. Small petechial haemorrhages could be made out on the surface. On the cut surface the cortex was found distinctly narrow and opaque. The mucous

[8] Measured from base of trabeculae carneae to outer surface

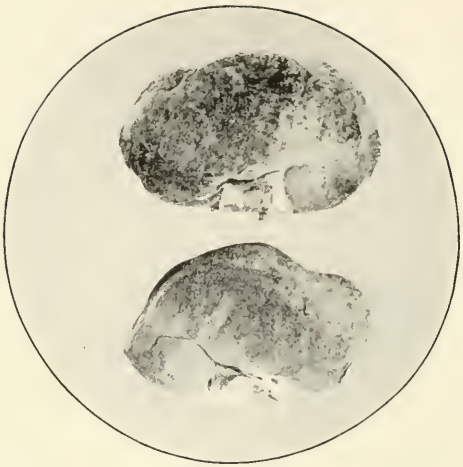

Fig. 29.

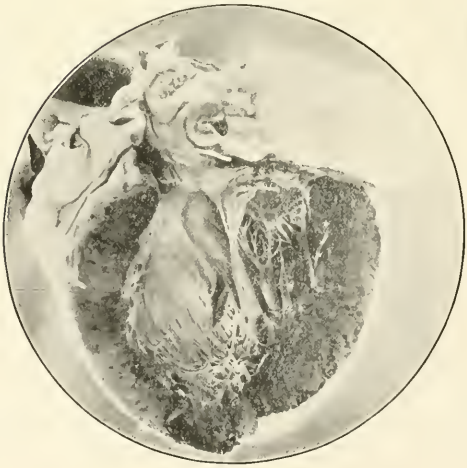

Fig. 30.

membrane of the renal pelvis and of the bladder was hyperaemic. Few diplococci were found in smears from the renal pelvis. Few diplococci were found in smears from the kidney tissue.

Microscopical sections showed a subacute and chronic diffuse intra- and extra-capillary glomerulo-nephritis, marked cellular infiltration and fibrous thickening of the interstitial tissue, with atrophy of many tubules; many neutrophilic leucocytes, much epithelial degeneration, and many

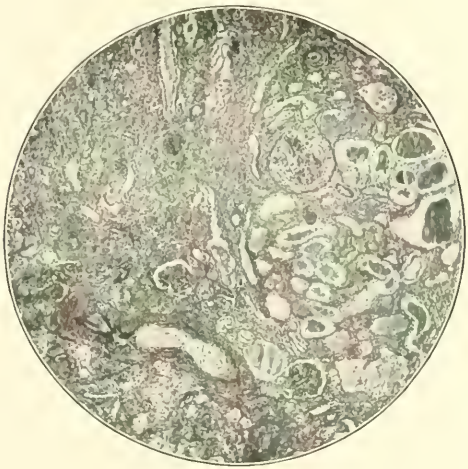

Fig. 31.

casts. Diplostreptococci were found in many capillaries and in the inflamed connective tissue near them; none were seen in the glomeruli or elsewhere. Many arterioles were either filled or lined on the inside with hyaline thrombus; sometimes these hyaline masses were found above, sometimes underneath the endothelial lining. In other arterioles there was a marked endarteritis, probably as a result of organization of these hyaline masses; others again showed a marked "arteriosclerosis." The large arteries showed a marked "arteriosclerosis."

Case 17. Chronic glomerulo-nephritis in man of 48 years with a history of scarlet fever and rheumatism.

XVI, 257.— J. McL., fairly well nourished Scotch butcher, 48 years old.

Patient had scarlet fever as a child, rheumatism at about the age of 20. Eight years before death he had pleurisy. For the last two and one-half years he had often had chills in the evening and night sweats; since that time he had also noticed shortness of breath and oedema. One year before death he observed puffiness of the face. At times he had

Fig. 32.

slight pains around the heart, radiating toward the arms. He complained of failing eyesight and frontal bilateral headaches. For these complaints he had been at the hospital off and on, where a peripheral arteriosclerosis, a cardiac enlargement with systolic and diastolic murmurs, was made out, and a severe anaemia (3,000,000 reds, 50% Hb.). He had a negative Wassermann reaction. Eight months before death his blood pressure was 200. At his last entrance it was 210, gradually falling to 165. Eight months before his death, examination of the fundus of the eyes showed an old disseminated syphilitic choroiditis, well defined arteriosclerosis, and evidence of former optic neuritis. The last

month he was more or less unconscious, at times delirious and noisy, and towards the end had several uraemic convulsions. While at the hospital his temperature and pulse were normal. He had had nycturia (six to seven times a night) for several years. His urine was greatly increased in quantity, to two liters and more, showed a fixed low specific gravity, contained much albumin and usually many hyaline and granular casts, and many leucocytes.

Necropsy revealed a large heart, twice the size of the fist; general oedema and hydrothorax; a marked general arteriosclerosis, and almost complete closure of the right coronary artery. The kidneys were of about normal size, granular.

Sections showed very marked, diffuse chronic and subacute intracapillary glomerulo-nephritis, with unusually extensive hyaline necroses of the vascular loops; many large areas of cellular infiltration, and marked diffuse cicatrization with atrophy of many tubules; few granular leucocytes; casts in many tubules; leucocytes in some. There was some fatty degeneration and necrosis of the epithelium; and hyaline masses in many small arteries causing sometimes complete obstruction. Marked "endarteritis" and marked "arteriosclerosis" were found both in the small and in the large arteries. The sections were badly contaminated with colon bacilli.

Case 18. Chronic glomerulo-nephritis with recent exacerbation, in man of 45, of unknown etiology.

XVI, 212.— A. L., well nourished Danish male cook, 45 years of age.

The history is imperfect, because the patient entered the hospital in a dazed condition and could not give a clear account of himself. He claimed to have been suffering for about two years from headache, dizziness, loss of memory, failing eyesight, shortness of breath, progressive weakness, and frequent urination. He never had oedema.

Clinical examination showed symptoms suggestive of partial sensory aphasia, a marked peripheral arteriosclerosis, enlargement of heart with accentuation of second aortic tone, lessened reflexes on the left side of the body, and horizontal nystagmus to the left. His blood was normal except for a slight leucocytosis (11,000 whites, 82% neutrophiles). The Wassermann reaction was negative on repeated tests, both in blood and spinal fluid. His blood-pressure was constantly very high, varying from 235 to 280. He had a retinitis albuminurica; towards the end he had convulsions. Shortly before death a petechial rash developed in the skin on hands, chest, and back. Towards the last there was some oedema of

the eyelids. He died in uraemic coma. His urine was increased in quantity, pale, clear, of low specific gravity, and contained much albumin, many hyaline and granular casts.

Necropsy revealed a heart which was somewhat enlarged (about one and one-fourth normal size), with small scars in the wall of the

Fig. 33.

left ventricle. There was a rather well marked general arteriosclerosis involving aorta, cerebral and coronary arteries, the small arteries in spleen and pancreas, and many others.

The kidneys were small (11 x 5 x 3 cm.) and full of small haemorrhages. The cortex was quite narrow, hyperaemic, and opaque.

Sections showed marked diffuse chronic and subacute glomerulonephritis (intra-capillary), with hyaline necroses in vascular loops; large areas of cellular infiltration, and fibrous thickening of the connective tissue with atrophy of tubules; blood and leucocytes in many tubules; much epithelial degeneration, few casts; marked thickening of intima both in small and in large arteries, partly with hyperplastic development of elastic tissue, partly without. The sections also showed numerous small old necrotic foci,—situated near badly affected glomeruli with thrombotic obstruction of vasa afferentia,—in which the capillaries were

hyperaemic, and showed much fibrin in and near them, which became hyaline eventually. Many granular leucocytes were found in and about such foci. Some of them showed beginning organization. No bacteria were detected in sections, in spite of especially careful search.

Case 19. Chronic glomerulo-nephritis in man of 37 years. No old septic focus found, but a diplostreptococcic infection of the rectum of unknown duration, and a terminal(?) diplostreptococcic sepsis.

XVI. 10.— J. M., well nourished Mexican sailor, 37 years of age

Patient claims to have always been healthy and well, denies any diseases of childhood. He suffered from "asthma," for the first time four years before entrance. Two months before death he had aching pains in neck, back, and extremities, which were worse at night. He had a syphilitic history and a positive Wassermann reaction. Clinical examination showed an enlargement of the heart and a soft systolic murmur, ascites, proctitis, general oedema. Towards the end he developed a marked dyspnoea. There were no definite uraemic symptoms. His temperature showed slight occasional rises, and his pulse varied from 80 to 100. His blood pressure was 182. He had a marked anaemia (2,350,000 reds; 50% Hb.), and on entrance to the hospital (two months before death) a leucocytosis (18,000), which disappeared later. His urine contained a moderate amount of albumin, few hyaline and granular casts, and later many red cells.

Necropsy revealed a muco-purulent proctitis due to diplostreptococcic infection. Few diplostreptococci were found in liver, spleen, kidneys, and lungs. There was also a terminal parotitis. The heart was one and one-half times normal size, with a very marked concentric hypertrophy of the left ventricle (14 mm.). The arteries, including the cerebral arteries, were normal, except the renals, which showed a marked arteriosclerosis. There was also present a general oedema, ascites, hydrothorax, and a cyanotic atrophy of the liver.

The kidneys were small (10 × 5 × 3½ cm.), the surface was finely granular, mottled purple and grey. No haemorrhages were seen. The cortex was moderately narrowed and opaque; the markings were poor

Sections showed mostly chronic glomerulo-nephritis; recent hyaline necroses in few glomeruli; large areas of cellular infiltration and cicatrization with atrophy of tubules; few granular leucocytes; some tubules filled with casts, blood and leucocytes. The epithelium was filled with

Fig. 34.

Fig. 35.

pigment in places and showed much fatty and granular degeneration. Hyaline deposits in the walls of many small arteries, apparently under

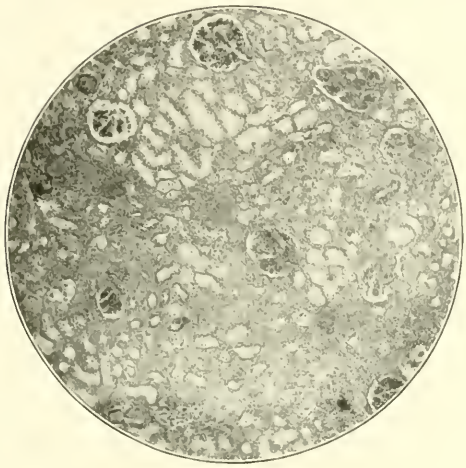

Fig. 36.

neath endothelium. Beginning "endarteritis" in the small arteries connected with diseased glomeruli, moderate "arteriosclerosis" in the larger arteries. No bacteria were found in sections.

Case 20. Chronic glomerulo-nephritis in Japanese of 35 years with old diplostreptococcic infection of tonsils.

XVIII, 167.— M., strongly built, well nourished Japanese farmer, 35 years of age.

Patient was admitted to hospital five days before his death, complaining of pains all over body, and of drowsiness. The first symptoms of renal disease were observed four years before, when he had general oedema and ascites, and was told that he had kidney disease. Two months before death swelling returned slightly, but disappeared again, since then he noticed shortness of breath and pains all over the body. For some days before admission he had headache, and vomited several times. Clinical examination showed semi-stupor, considerable puffiness around the eyes, heavily coated tongue and foul breath, normal heart-

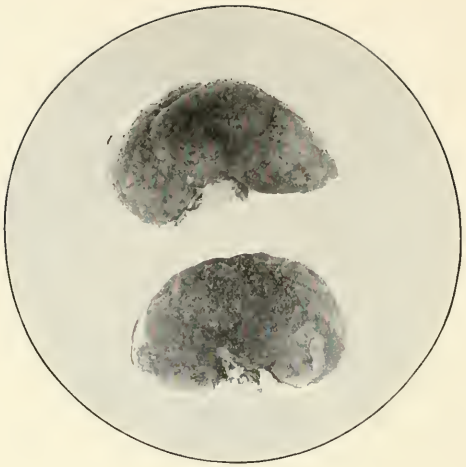

Fig. 37.

Fig. 38.

dullness, systolic murmur at base, accentuated second aortic tone, marked general hyperaesthesia, especially of muscles, and scaly skin. The temperature was normal. His pulse rate was rather slow, averaging about 64. His blood-pressure, during the last days of his life, was 115. He had a severe anaemia (2,804,000 reds; 43% Hb.) with poikilocy-

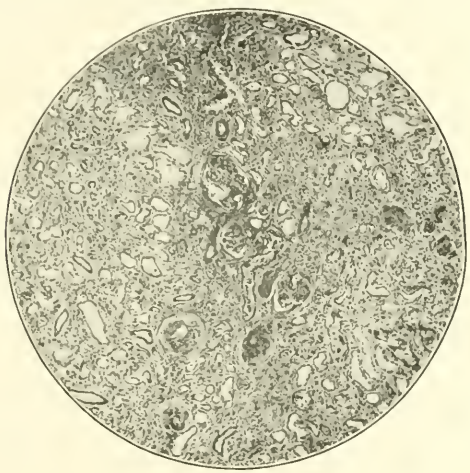

Fig. 30.

tosis and anisocytosis and some leucocytosis (18,000). The Wassermann reaction was negative both in blood and spinal fluid. Towards the end the patient had occasional attacks of severe dyspnœa, in one of which he died (uraemia). His urine was of low specific gravity (1010), contained much albumin, and in one specimen many granular casts and leucocytes.

Necropsy revealed chronic tonsillitis with old pus pockets in crypts (diplostreptococcic infection). The heart was about one and one half times normal size (left ventricle not dilated, averaged 12 mm.). The aorta was markedly atheromatous; the other arteries, including renals, were normal.

The kidneys were small (9½ × 4½ × 3½ cm.). The capsules were thickened and adherent. The surface was somewhat rough and quite pale. On the cut surface the cortex was distinctly narrowed (to 2–3 mm.) and opaque.

Microscopic sections showed diffuse, chronic, intra-capillary glomerulo-nephritis, more subacute lesions in few glomeruli, marked diffuse fibrosis with large areas of cellular infiltration, some of which contain many neutrophilic and basophilic leucocytes, marked atrophy of many tubules, compensatory enlargement of others, little epithelial degeneration, blood and leucocytes in many tubules, also many hyaline casts, slight "arteriosclerosis" of arterioles in most fibrous areas, moderate "arteriosclerosis" of larger ones. No bacteria were found in the sections, in spite of careful search.

Case 21. Chronic glomerulo-nephritis in woman of 36 with old scar in base of aorta, old pericarditis, septic thrombosis of left auricle, and old septic infarct in spleen containing influenza bacilli.

XVI, 260.— Mrs. K., emaciated English housewife, 36 years of age.

Patient's health was good until she was 22, when she had a severe infection ("touch of typhoid"). Since she was 23 years old, she had spells of intense headache, vomiting, nausea, and occasional nose-bleeds. She had oedema at times. Eight years before death, premature delivery in eighth month of pregnancy became necessary on account of albuminuria. Before the birth of her second child, two years later, there was much oedema. She suffered much from severe dyspnoea, pains over heart and kidneys, and sleeplessness. In the last months she had much stomatitis and tonsillitis. Towards the end she was very weak, restless, and delirious (uraemia). The pleurae had to be tapped several times for hydrothorax. She had a marked anaemia (3,500,000 reds; 65% Hb.) and a normal leucocyte count. Her temperature was normal, her pulse rate quite varying, sometimes increased to 120 or over. Her respiration was about 30. Her blood-pressure varied between 160 and 190. She urinated once at night. Her urine on frequent examination had a low specific gravity and contained a heavy cloud of albumin (0.5% or over), many granular and hyaline casts; blood was found on one occasion. Phenolsulphone-phthalein was slowly excreted (20 resp. 11% first hour, 15 resp. 21% second hour).

Necropsy revealed an old scar in one of the sinus Valsalvae, a healed pericarditis, septic thrombi in left ventricle and left auricle, an old septic infarct in spleen (many influenza bacilli in thrombi and in infarct), marked oedema and slight hydrothorax. The heart was one and one-half times normal size. The left ventricle measured 13 mm., and was

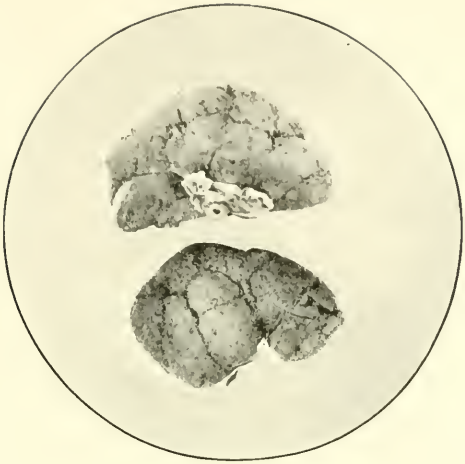

Fig. 40.

Fig. 41.

firm. The renal arteries were moderately sclerosed, the others practically normal.

The kidneys were small (10 x 5 x 3 and 8½ x 4½ x 2½ cm. resp.); the capsule was adherent; the surface distinctly granular; the cortex much reduced (to 3 mm. in places). The tissue was soft, oedematous,

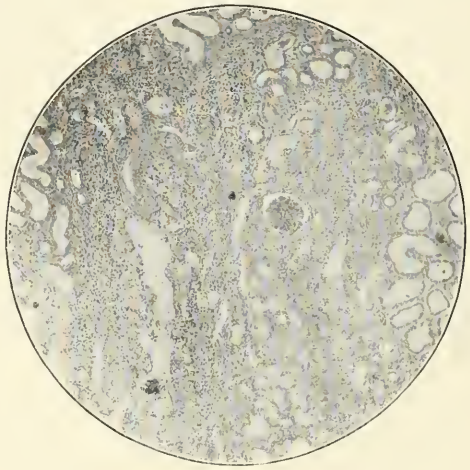

Fig. 42.

and full of opaque spots. There were few haemorrhages in the cortex of the right kidney.

Sections show mostly chronic, but also some recent, glomerulonephritis (intra-capillary); large areas of cellular infiltration and fibrous thickening of the connective tissue with atrophy of tubules; few granular leucocytes; little blood in tubules; granular and fatty degeneration of the epithelium, moderate number of casts; much hyaline underneath endothelium in several small arteries; marked "endarteritis" of the small arteries and moderate "arteriosclerosis" of the larger ones. No pathogenic bacteria were seen in sections.

Case 22. Chronic glomerulo-nephritis in man of 42 years with old tuberculosis and continued suppuration of the lymph-glands of the neck.

XVII, 184.— R. M., poorly nourished Scotch clerk, 42 years of age.

Patient had had chronic tuberculosis of lymph-glands of neck since childhood, which necessitated twelve operations. For the last three years before entrance he had had occasional nycturia; for the past three weeks he had been easily fatigued, and suffered from indigestion; and

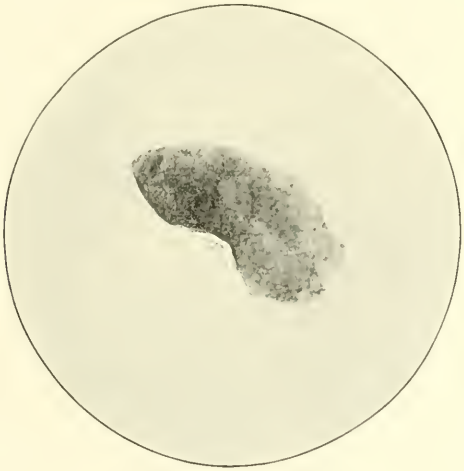

Fig. 43.

for the past ten days he noticed shortness of breath, œdema of legs, and oliguria. On clinical examination he showed a very marked dyspnœa and cyanosis, very poor teeth, slight enlargement of heart, a soft systolic murmur at apex, petechiae on right arm and left thigh, marked œdema of lower extremities. The peripheral arteries appeared sclerotic. Later he developed pericardial friction and signs of pleurisy. Towards the end the patient was very dyspnœic and drowsy, sometimes delirious, and showed muscular twitching. He died in uraemic coma. He was anaemic (3,160,000 reds; 62% Hb.); he had a leucocytosis (14-25,000 leucocytes, 90% neutrophiles). His blood-pressure varied from 200 to 235.

Fig. 44.

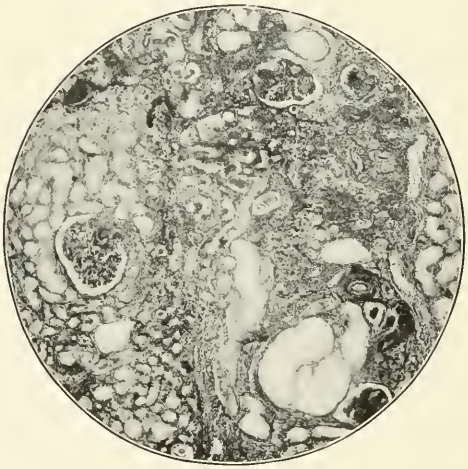

Fig. 45.

His temperature was subnormal (97° F.), with rises to 99° F. His urine while at hospital was scanty, of low specific gravity, and contained much albumin, many hyaline, epithelial, and granular casts; no blood was found.

Necropsy revealed numerous old scars on neck and slight remnants of old tubercular infection, recent haemorrhagic diplostreptococcic pericarditis and pleurisy, broncho-pneumonia. The heart was one and one-half times normal size (left ventricle averaged 14 mm.). The renal arteries were moderately sclerosed, the others practically normal.

The kidneys were small (10 x 4 x 3 cm.), the capsule firmly adherent, surface granular, small haemorrhages in cortex, which was much reduced (4 mm.). The markings were indefinite.

Sections showed chronic glomerulo-nephritis in the majority of the glomeruli; more recent changes in a few; diffuse cicatrization with small areas of cellular infiltration; few granular leucocytes; many casts in collapsed tubules; leucocytes in some of the tubules; little epithelial degeneration; hyaline in few small arteries; marked "endarteritis" in many small arteries; marked "arteriosclerosis" in few small and all larger arteries. No pathogenic bacteria were found in sections.

Case 23. Chronic glomerulo-nephritis in man of 55 with chronic endocarditis.

XVII, 116.— J. H., well nourished Canadian sailor, 55 years of age.

Patient had repeated attacks of tonsillitis, was in hospital three years before death for rheumatism; reëntered shortly before death with acute rheumatism of hands. There was no history of syphilis. The Wassermann reaction was negative. Patient had "epileptic" attacks at various times, last one three months before death. He complained of shortness of breath, increasing dimness of vision, cramps in legs, and deep pains in bones. He never had any oedema.

Clinical examination showed marked nervousness, hacking cough, contracture in left leg, arteriosclerosis of radial artery, heart within normal limits, a soft systolic murmur, no oedema. The backgrounds of his eyes showed small, slightly tortuous arteries, otherwise they were normal. Towards the end he had bleeding from nose and mouth, vomited daily, and developed uraemic coma. His blood-pressure varied from 190 to 210. He had a severe anaemia (2,150,000 reds; 30% Hb, anisocytosis), no leucocytosis. His temperature was subnormal. His pulse rate varied between 70 and 95. His urine was scanty, of low specific gravity,

contained much albumin, many granular casts, few leucocytes, few red cells.

Necropsy revealed an old endocarditis of the mitral valve. The heart was somewhat enlarged. There was a terminal broncho-pneu-

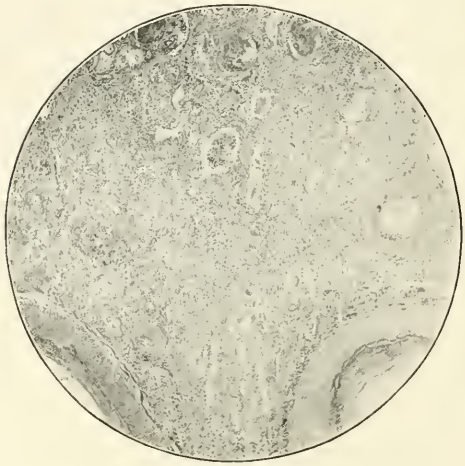

Fig. 46.

monia. The radial artery showed a marked arteriosclerosis; the others were much less involved.

The kidneys were small and pale; the capsule adherent, surface granular, cortex narrow, full of cysts.

Sections show chronic glomerulo-nephritis in many glomeruli (intracapillary), more recent lesions in few; very extensive cicatrization of cortex with much cellular infiltration; few granular leucocytes; much epithelial degeneration and many casts; leucocytes in few tubules; much subendothelial hyaline in many small arteries; marked "endarteritis" in most small arteries, more "arteriosclerotic" lesions in others; very marked "arteriosclerosis" of larger arteries. No pathogenic bacteria were found in sections.

Case 24. Chronic practically healed glomerulo-nephritis in man of 61 with old history of rheumatism.

XVII, 164. D. G., emaciated French male cook, 61 years of age.

Patient had rheumatism when he was young. He denied all venereal disease. His present illness began two years ago with loss of weight (35 lbs.), shortness of breath, and increasing weakness. He had to void his urine at night two to three times.

Clinical examination showed a marked puffiness of skin about eyes, much dyspnoea, coated tongue, and foul breath, enlarged heart, a rough

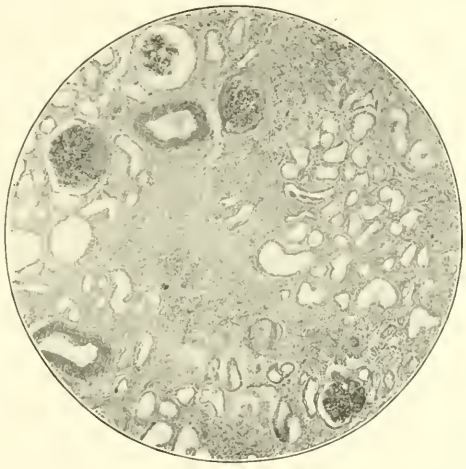

Fig. 47.

systolic and faint diastolic murmur over the heart. The rhythm of the heart was absolutely irregular. His liver was enlarged. His blood-pressure on entrance was 170, later gradually went down to 137. Patient had no marked oedema at any time. He had a severe anaemia (3,500,000 reds and 48% Hb.), also a slight leucocytosis (14,600). The Wassermann reaction was negative. The urine was scanty at first, later about normal in quantity. The specific gravity was about 1010. It contained considerable albumin, and at times many granular casts and red cells. The patient at no time showed definite symptoms of uraemia. He died with the clinical symptoms of an acute pulmonary infection.

Necropsy revealed marked general arteriosclerosis, a very marked enlargement of the heart (about three times normal size), small scars in heart muscle, gouty deposits in kidneys and toe joints, a terminal broncho-pneumonia, beginning cyanotic atrophy of liver.

The kidneys were small (10½ x 4 x 4 cm.); the capsule stripped easily. The surface was coarsely granular. The cortex was much reduced, and the markings were very indistinct.

Sections show chronic glomerulo-nephritis in many glomeruli with large areas of cicatrization in cortex, comparatively little cellular infiltration, few granular leucocytes; subacute glomerulo-nephritis (intra-capillary) in few glomeruli; leucocytes in few tubules; little epithelial degeneration; very marked "arteriosclerosis" of large and small arteries. No bacteria were found in sections.

Case 25. Chronic glomerulo-nephritis, in man of 60 years, of unknown etiology.

XVIII, 108.— T. H. D., poorly nourished man, 60 years of age.

No history could be obtained on account of the condition of the

Fig. 48.

patient. Patient entered the hospital in a delirious condition. He showed a coarse tremor of the extremities, a jerking of the head, and consider-

able rigidity of the neck. The reflexes were exaggerated. There was an infected wound over the occiput. His temperature ranged between 97.6° and 99.5° F. His pulse was high and irregular. He had no oedema. He died three days later in coma.

Necropsy revealed a beginning prostatic hypertrophy and terminal broncho-pneumonia. His heart was of normal size. There was a slight concentric hypertrophy of the left ventricle. All arteries, the aorta and cerebral vessels included, showed a marked arteriosclerosis.

The kidneys were small (9.7 x 4 x 2.3). The capsule stripped with difficulty. The surface was granular. The cortex was narrow and opaque. There were no visible haemorrhages.

Microscopical sections showed very extensive old glomerulo-nephritis of many glomeruli, much cellular infiltration and fibrous thickening of the connective tissue with atrophy of groups of tubules, much epithelial degeneration, many casts and leucocytes in tubules, considerable pigmentation of the epithelium. The arterioles and the larger arteries showed a very marked "arteriosclerosis."

Case 26. Chronic glomerulo-nephritis, in man of 54 years, of unknown etiology.

XVIII, 19.— S. G., emaciated Irish teamster, 54 years of age.

Patient did not recall any diseases except measles in infancy. He was a heavy beer drinker. He had gonorrhoea at 35, denied lues. Five years before death he became dropsical for the first time; he had another attack one year ago, associated with "rheumatism." He complained of dropsy, shortness of breath, palpitations, and precordial pain, headache, and pains in legs.

Clinical examination showed marked drowsiness, marked oedema of face, coated tongue, poor condition of few remaining teeth, enlargement of heart, distant heart sounds but no definite murmurs, ascites, general oedema. Towards the end he became delirious, and died in uraemic coma. His blood-pressure varied between 190 and 210. He had some anaemia (78% Hb.), no leucocytosis. His temperature was normal and at times subnormal. His pulse rate varied between 80 and 130. His urinary output varied between 1400 and 2500 ccm. daily. The specific gravity was low. The urine contained a heavy cloud of albumin, occasional hyaline casts, few leucocytes, no blood. There was practically no excretion of phenolsulphone-phthalein.

Necropsy revealed a slightly enlarged heart (left ventricle averaged 12 mm.), marked arteriosclerosis of coronaries and of all abdominal arteries, cyanotic atrophy of the liver, much oedema, ascites and hydro-

thorax, recent haemorrhagic pericarditis without bacterial findings. He also had gouty joints.

The kidneys were small (8½ x 3½ x 3 cm.); the capsule was thick and adherent; the surface granular. The cortex was much reduced (to about 3 mm.) and full of cysts; the markings were poor.

Sections showed chronic glomerulo-nephritis in many and subacute lesions in few glomeruli; large areas of cellular infiltration and fibrous

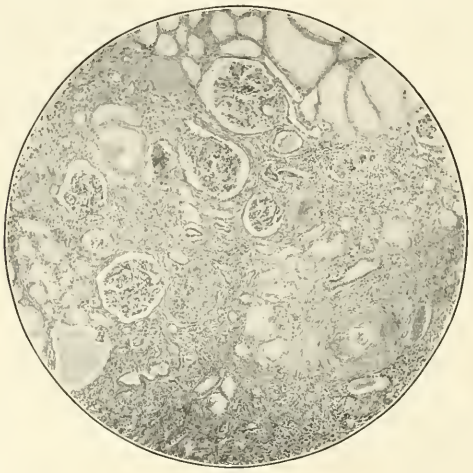

Fig. 49.

thickening of the connective tissue with atrophy of the tubules; moderate infiltration with neutrophilic leucocytes, few eosinophiles and basophiles; slight epithelial degeneration, many casts in atrophic tubules; subendothelial hyaline in few small arteries; marked "arteriosclerosis" and "endarteritis" in small arteries, marked "arteriosclerosis" in large arteries. No bacteria were found in sections.

Case 27. Chronic glomerulo-nephritis in man with old "malaria" and terminal septic lesions.

XVII, 82.— C. S., well nourished American male nurse, 31 years of age.

The history is imperfect. "He had 'malaria' two and one-half years ago which was recurrent." He had syphilis at the age of 26, and several attacks of gonorrhoea.

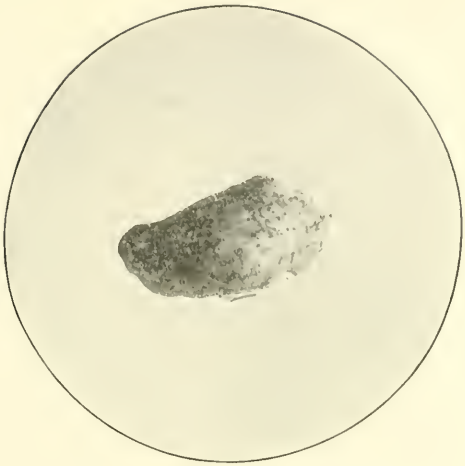

Fig. 50.

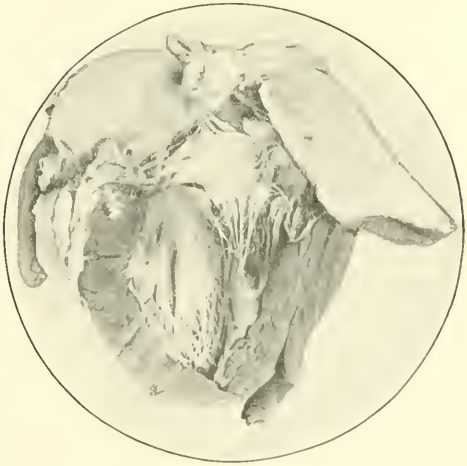

Fig. 51.

Necropsy revealed an ulcerative diplostreptococcic stomatitis, an acute suppurative pericarditis without bacterial findings, and an acute endocarditis of the mitral valve. The heart was one and one-fourth times normal size, and the left ventricle averaged 15 mm. There was a marked arteriosclerosis of the aorta, coronaries, splenic, renal, and cere-

Fig. 52.

bral arteries. The liver showed cyanotic atrophy with compensatory hypertrophy of the peripheral parts of the lobules.

The kidneys were small (8½ x 4 x 3 cm.) and granular, showing grey spots on a red background. There were many haemorrhages in the cortex. The latter was much reduced. Some gouty deposits were found in the pyramids.

Sections showed chronic glomerulo-nephritis of most glomeruli and more subacute lesions (intra-capillary) in a few; almost total destruction of the cortex by fibrosis, much cellular infiltration; few granular leucocytes; blood and leucocytes in many tubules, much epithelial degeneration, many casts: "endarteritis" in few small arteries, very marked "arteriosclerosis" in the rest. No bacteria were found in sections.

Case 28. Chronic glomerulo-nephritis in man of 24 years with chronic endocarditis.

XVII, 140.—L. A., well nourished Italian boxmaker, 24 years of age.

The patient's general health had been good until one year before his death, when he had rheumatism in feet and hands. His present illness started four months ago with epistaxis, shortness of breath and pain in the epigastrium.

Clinical examination showed continued bleeding from nasal mucous membrane, a heavily coated tongue, very marked dyspnoea in spite of comparatively little circulatory disturbance (uraemic air hunger), mod-

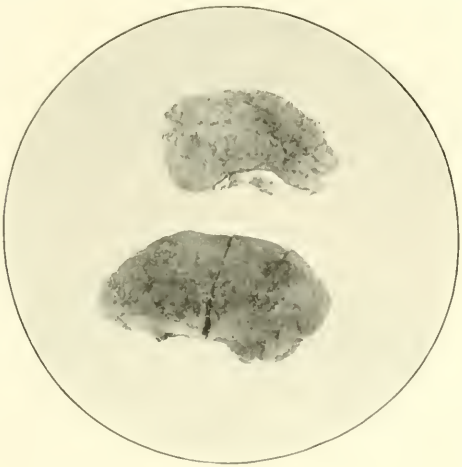

Fig. 53.

erate dilatation of the heart towards the right, a presystolic murmur, normal rate and rhythm of heart beat. Patient had no oedema at any time. He had a severe anaemia (3,100,000 reds; 48% Hb.); towards the end much leucocytosis (30,000; 93% neutrophiles). Blood culture was negative. His temperature was subnormal. For the last one and one-half months he voided urine four to five times at night. It was of low specific gravity (1011) and contained much albumin; no casts. (One examination, as patient was in hospital one day only.) No coma.

Fig. 54.

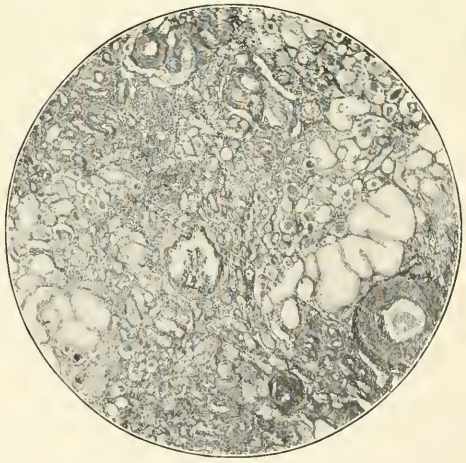

Fig. 55.

Necropsy revealed an old endocarditis of the mitral valve with moderate stenosis (no bacteria found), recent apparently embolic pustules on chin and left hand, a heart of normal size on the left, slight dilatation on the right side; an old primary tuberculosis of the intestines and of the mesenteric lymph-glands. The arteries were normal.

The kidneys were small ($9\frac{1}{2} \times 4\frac{1}{2} \times 3$ and $7 \times 4 \times 2\frac{1}{2}$ cm., respectively). The capsule was adherent; surface coarsely granular, cortex very narrow, opaque, very light in color, almost yellow.

Sections show chronic glomerulo-nephritis in many glomeruli, more recent changes (intra-capillary) in few; large areas of fibrosis with atrophy of tubules; few areas of cellular infiltration; considerable number of eosinophiles, fewer neutrophiles and basophiles; many casts, few leucocytes in some tubules; little epithelial degeneration; marked "endarteritis" of small arteries, slight "arteriosclerosis" of the larger ones. No bacteria were found in sections.

Case 29. Chronic glomerulo-nephritis in man of 59 years with possibly old septic focus in urinary tract.

XVI, 189.— S. G., emaciated Chinese male cook, 59 years of age.

The history is incomplete, because patient did not speak English. He had noticed puffiness of the face, shortness of breath, palpitation and pain over heart, and swollen legs for the last four to five months. He vomited occasionally, but had no headaches. Clinical examination showed poor teeth, a normal heart, and oedema of the lower extremities. He had a very marked anaemia (2,100,000 reds; 35% Hb.), no leucocytosis. His temperature was subnormal. His pulse rate varied between 60 and 80. The urine (one examination) contained a moderate amount of albumin, no casts, many epithelial cells, and few leucocytes.

Necropsy revealed a small heart, normal arteries except some atheroma of the aorta and moderate arteriosclerosis of the renal arteries, beginning cyanotic atrophy of liver, general oedema, marked ascites and hydrothorax; gouty deposits in ears, basal joints of great toes, and kidneys; purulent cystitis and prostatitis.

The kidneys were very small ($8 \times 3\frac{1}{2} \times 2\frac{1}{2}$ and $7 \times 3\frac{1}{2} \times 2\frac{1}{2}$ cm., respectively); the capsule was adherent, the surface granular, the cortex very narrow (2-3 mm.).

Sections showed chronic glomerulo-nephritis of most glomeruli, more sub-acute lesions (intra-capillary) in others, considerable hyaline necrosis in affected glomeruli; very extensive cicatrization of cortex

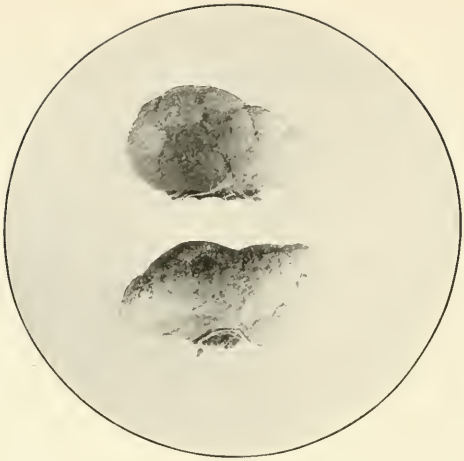

Fig. 56.

Fig. 57.

with some areas of cellular infiltration; very few granular leucocytes, much epithelial degeneration; very many casts, blood in some tubules.

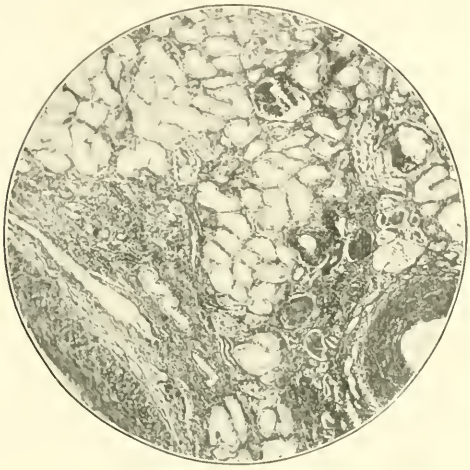

Fig. 58.

very marked "arteriosclerosis" of the small arteries, less in the large ones. No pathogenic bacteria were found in sections.

Case 30. Chronic glomerulo-nephritis in man 38 years of age with a history of repeated attacks of tonsillitis.

XV, 33.— J. C., strongly built boilermaker and bartender, 38 years old.

Patient had been subject to strain and bad weather for twenty-five years. He had frequent attacks of sore throat and many colds. He had used alcohol to excess. He had gonorrhoea and chancroid at 24. When he was 30 he had an attack of "rheumatism" in the right great toe, about one year before his death he had "rheumatism" in several joints and facial palsy following pain at base of skull. Clinical examination showed marked anaemia, coated tongue, bad teeth, heart within normal limits, no murmurs. No oedema. At the hospital he had a fit of "epilepsy." He had a suspicious Wassermann reaction. His blood-pressure was 160. He had a severe anaemia (2,700,000 reds; 35% Hb, no leuco

cytosis). His temperature was slightly subnormal. His pulse rate varied from 84 to 100. The last three days he had continued epistaxis. He had to void urine frequently and to get up several times at night. Urinanalysis (one examination) showed specific gravity of 1023, no albumin, few granular casts, leucocytes and erythrocytes.

Necropsy revealed purulent bronchitis and broncho-pneumonia, haemorrhagic pleurisy and pericarditis. The heart was slightly enlarged

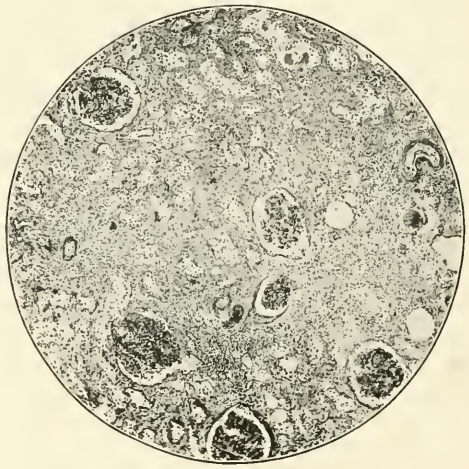

Fig. 59.

(left ventricle averaged 12 mm.). The blood-vessels were practically normal. There were gouty deposits in toe joints and kidneys.

The kidneys were small (9½ x 4 x 2½ cm.) and granular. The cortex was much reduced, and the markings were indefinite.

Sections show chronic glomerulo-nephritis in the majority of the glomeruli, more subacute lesions (intra-capillary) in the few remaining ones, very marked diffuse cicatrization of cortex—with little cellular infiltration; few small, fairly intact areas of kidney tissue; much epithelial degeneration, many small epithelial cysts; blood and leucocytes in few tubules; hyaline masses in few small arteries; marked "arteriosclerosis" of many arterioles; moderate "arteriosclerosis" in larger arteries.

Case 31. Chronic glomerulo-nephritis in woman of 28 years with old ulcer of tonsil and chronic diplostreptococcic infection of urinary tract.

XVII, 68.— Mrs. G. E., emaciated American domestic, 28 years of age.

Patient had always been in poor health; had "La Grippe" as a girl; had had chronic catarrh for many years. Nine years before death appendectomy was performed for acute appendicitis. She had kidney

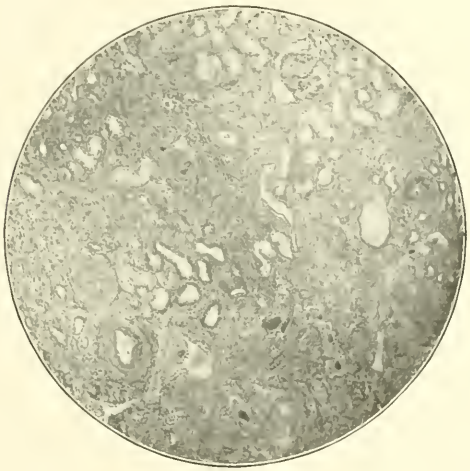

Fig. 60

trouble while carrying her first child, five years before death, again when carrying the second. About one year before death she noticed progressive debility with anorexia and vomiting. A little later she had some attacks of violent delirium with complete unconsciousness. She voided much pale urine. For the last seven months she had headache, vomiting, jerking and cramps in legs, palpitations of the heart, progressive weakness and loss of weight, progressive amaurosis, and at times oedema of the feet; towards the end patient was very noisy, restless, and delirious.

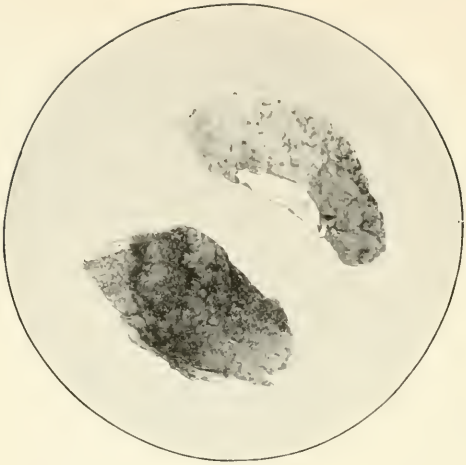

Fig. 61.

Fig. 62.

Her tongue was heavily coated and her breath uraemic. Her temperature was normal, her pulse varied greatly (between 80 and 120). Ophthalmoscopic examination showed an albuminuric retinitis. Her blood-pressure was 185. She died in uraemic coma. She had a marked anaemia (2,700,000 reds; 40% Hb.), some leucocytosis (14,000), 80% neutrophiles. The Wassermann reaction was negative. The phenolsulphone-phthalein excretion was diminished (1. hour 5%; 2. hour 25%). The urine was increased in quantity, of low specific gravity (1010 or less), contained much albumin (to 2%), occasional showers of casts, few red cells, and few leucocytes.

Necropsy revealed a heart about one and one-half times normal size (left ventricle averaged about 11 mm.), normal blood-vessels, an old ulcer of the tonsil, chronic diplostreptococcic cystitis and pyelitis (diplostreptococci also found in right kidney), haemorrhagic fluid in both pleurae and terminal broncho-pneumonia.

The kidneys were very small, especially in antero-posterior diameter (9 x 4 x 3 cm.), coarsely granular, full of large retracted scars; the cortex was very narrow and full of opaque spots.

Sections showed mostly chronic glomerulo-nephritis, more recent lesions in few glomeruli (intra-capillary); large areas of cicatrization with much cellular infiltration; few granular leucocytes; moderate epithelial degeneration; many casts, blood and leucocytes in some tubules; marked "arteriosclerosis" of small, less so of large arteries. No bacteria were found in sections.

Case 32. Chronic glomerulo-nephritis in man of 24 years with indefinite septic history.

XV. 07.— G. A., emaciated Canadian jockey, 24 years of age.

History imperfect. Patient when a boy had "malaria" several times, a definite attack of rheumatism one year before death. When 19 he had a chancre without secondaries. He had been losing weight, had frequent nose-bleed, and was markedly anaemic. His temperature was subnormal.

Necropsy revealed a rather small heart, normal blood-vessels, slight ascites, more marked hydrothorax, no subcutaneous oedema, and terminal broncho-pneumonia.

The kidneys were very small ($8\frac{1}{2}$ x $3\frac{1}{2}$ x 2 and $7\frac{1}{2}$ x $3\frac{1}{2}$ x 3 cm., respectively); the capsule was firmly adherent; the cortex was thin and opaque, and full of yellow spots.

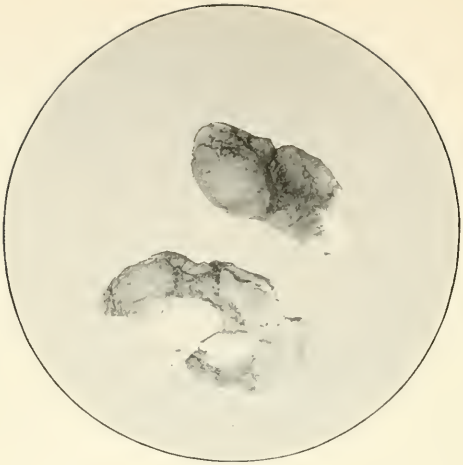

Fig. 63.

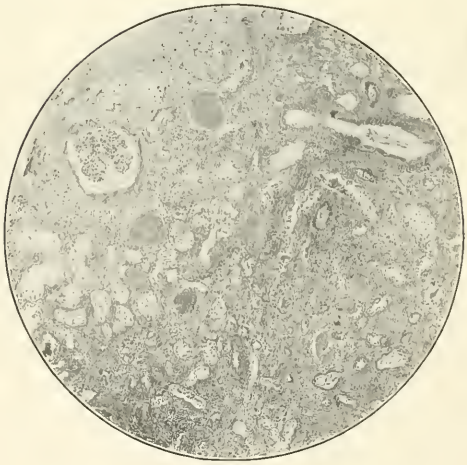

Fig. 64.

Sections showed chronic glomerulo-nephritis of practically all glomeruli,—much hyaline in the affected glomeruli; almost complete destruction of cortex by cicatrization, many large areas of cellular infiltration; much epithelial degeneration, moderate number of casts, blood, and leucocytes in some tubules; moderate "endarteritis" and "arteriosclerosis" in small vessels, slight "arteriosclerosis" in large ones. The sections were too badly contaminated to permit of bacteriological examination.

SUMMARY OF CASE

I. A

Case No.	Sex and Age	Etiology	Condition of Kidney
1. xvii, 60	M, 52	Diplostreptococcic endocarditis.	Swollen, opaque, few haemorrhage 6 x 3)
2. xvii, 31	M, 54	Diplostreptococcic endocarditis.	Normal size, many haemorrhages
3. xvii, 188	M, 41	Diplostreptococcic endocarditis.	Much swollen, opaque, few haemo (13 x 7 x 4½)
4. xviii, 158	F, 33	Streptococcic ulcers of legs.	Distinctly swollen, hyperaemic, oede (12½ x 6 x 4½)
			II. SUB
5. xviii, 166	F, 33	Diplostreptococcic endocarditis.	Swollen, many haemorrhages (12 x
6. xvi, 56	F, 2 mo.	Colon bacillus pyelitis.	Swollen, opaque
7. xvii, 163	M, 40	Diplostreptococcic endocarditis.	Swollen; cortex wide, opaque, many orrhages
8. xiv, 34	M, 45	Streptococcic infection.	Swollen, opaque, mottled, many h rhages (12 x 7 x 4)
9. xv, 135	M, 33	Diplostreptococcic endocarditis.	Normal size, cortex wide, opaque haemorrhages
10. xviii, 106	F, 27	Abscess of jaw.	Normal size, cortex wide, yellow,
11. xvii, 119	M, 51	Diplostreptococcic endocarditis.	Swollen, many haemorrhages, cortex
12. xviii, 61	F, 26	Tonsillitis	Slightly reduced in size, many h rhages (10½ x 4½ x 3)
			III. SUBACUTE AND CHR
13. xvi, 190	F, 8	Infectious aneurysm, diplostreptococcic.	Rt. kidney swollen, pale, opaque; le tracted (8 x 4 x 3½)
14. xvii, 17	F, 10	Tonsillitis.	Small, granular (6 x 3 x 2; 9 x 4 x 3 tex narrow
15. xv, 120	M, 6	Streptococcic cystitis and pyelitis.	Small, with large deep scars

ERULO-NEPHRITIS

RULO NEPHRITIS.

ndition of Urine			Hypertension and Cardiac Hypertrophy	Arteriosclerosis, Local and General	Oedema	Uraemia	Retinitis albuminurica	Anaemia
Casts	Erythrocytes	Leucocytes						
+++	—	—	—	loc.+ gen.+	card.	—	—	+
+	—	—	—	loc.+ gen.+	card.	—	—	+
+++	—	—	—	loc.+ gen.–	++	—	—	–
+++	—	+++	—	loc.+ gen.–	+	—	—	++

RULO-NEPHRITIS

+++	++	+++	—	loc.– gen.	+	+	—	++
?	—	—	—	loc.– gen.–	+	—	—	—
+	—	—	—	loc.– gen	+	—	—	–
+++	+++	+	Sl. hypert. of left ventricle?	loc.+ gen.+	+	—	—	++
+++	++	++	—	loc.– gen.–	+	—	—	++
+++	++	++	B.P 170; H. sl. h.	loc.+ gen.–	++	—	—	+
+++	++	++	B. P. 200; H. 2x	loc.+ gen.+	+	—	—	++
+++	++	+	B. P 180; H. n	loc.++ gen.++	++	+	+	++

RULO-NEPHRITIS IN CHILDREN.

+	—	+	B P 140; H 2x	loc. gen.–		+	?	+
+	+	—	B P 150; H. 2x	loc.+ gen.–	++	+	—	+
?	?	?	H hyp left.	loc.+ gen.–	—	+		+

Case No.	Sex and Age	Etiology	Condition of Kidney
16. xviii, 170	M, 53	Diplostreptococcus sepsis.	Normal size, slightly granular, r some haemorrhages
17. xvi, 257	M, 48	Rheumatism.	Normal size, granular
18. xvi, 212	M, 45	(?) History imperf.	Small (11 x 5 x 3), many haemor cortex narrow
19. xvi, 10	M, 37	Diplostreptococcus sepsis (?).	Small (10 x 5 x 3½), mottled; corte row, opaque
20. xviii, 167	M, 35	Tonsillitis.	Small (9½ x 4½ x 3½), pale; cort row, opaque
21. xvi, 260	F, 36	Old infection with influenza-bacilli	Small (9 x 5 x 3), granular, cortex opaque, few haemorrhages
22. xvii, 184	M, 42	Chronic tuberculosis and suppuration of glands	Small (10 x 4 x 3), granular; corte row, few haemorrhages
23. xvii, 116	M, 55	Old endocarditis	Small, pale, granular; cortex narrow
24. xvii, 164	M, 61	Rheumatism	Small (10½ x 4 x 4), granular; cort narrow
25. xviii, 108	M, 60	(?) No history	Small (10 x 4 x 2½), granular; cort row, opaque
26. xviii, 19	M, 54	(?)	Small (8½ x 3½ x 3), granular; narrow, cystic
27. xvii, 82	M, 31	(?) History imperf.	Small (8½ x 4 x 3), granular; many orrhages
28. xvii, 149	M, 24	Old endocarditis	Small (8 x 4 x 3), granular; cortex pale
29. xvi, 189	M, 59	(?) History imperf.	Small (8 x 3 x 2½), granular; corte narrow
30. xv, 33	M, 38	Tonsillitis	Small (9½ x 4 x 2½), granular; very narrow
31. xvii, 68	F, 28	Tonsillitis	Small (9 x 4 x 3), granular; corte narrow
32. xv, 97	M, 24	Old sepsis suspected	Small (8½ x 3½ x 2), granular; very narrow

Key to abbreviations: M, male; F, female; P, polyuria; B. P., blood-p
+++, marked; —, negative; ?, unknown or questionable. All measu

ndition of Urine			Hypertension and Cardiac Hypertrophy	Arterionecle-rosis, Local and General	Oedema	Uraemia	Retinitis albu-minurica	Anae-mia
Casts	Erythro-cytes	Leuco-cytes						
-	··	··	(?) H. $1\frac{1}{2}$S	loc. ·· gen.·	++	—	—	?
··	—	( )	B.P. 200. H. 2S	loc. — gen.··	··		?	++
—	—	—	B.P. 250. H. $1\frac{1}{4}$S	loc. ·· gen. ·	—	·		—
		-	B.P. 182. H. $1\frac{1}{2}$S	loc. · gen —	··		—	··
·	—	( )	B.P. 115. H. $1\frac{1}{2}$S	loc. · gen —	·	·	—	( )
++	—	·	B.P. 180. H. $1\frac{1}{2}$S	loc. · gen —	—		··	—
+++	—	—	B.P. 230. H. $1\frac{1}{2}$S	loc. ·· gen		·	—	·+
··		·	B.P. 260. H. $1\frac{1}{4}$S	loc — gen ·	—	( )	—	·+
-	—	—	B.P. 170. H. 3S	loc — gen —	—	—	—	··
?	?	?	B.P. (?); H. n	loc · gen ··	—	·	—	?
( )	—		B.P. 200. H. $1\frac{1}{4}$S	loc ·· gen.+··	·	+	—	+
?	?	·	B.P. (?); H. $1\frac{1}{4}$S	loc.··· gen.··		?	—	?
—	( )		B.P. (?); H. n.	loc gen.—	—	—	—	
—	—		B.P. (?). H. sm	loc ·· gen	··	·?	—	++
			B.P. 160. H. $1\frac{1}{4}$S	loc.+++ gen —	—	·	—	·+
			B.P. 185. H. $1\frac{1}{2}$S	loc gen	( )	( )	—	++
?	?		B.P. (?). H. sm	loc · gen —	+	( )	—	·

t; loc., local; gen., general; card., cardiac; +, slight; ·+, moderate;
meters.

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